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SYNDROME OF DIFFUSE MUSCULAR HYPERTROPHY IN INFANTS CAUSING ATHLETIC APPEARANCE

ITS CONNECTION WITH CONGENITAL MYXEDEMA

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In 1925, we had the honor of showing to the Pediatric Society of Paris [1] a baby 10 months old whose appearance seemed interesting. He presented a syndrome unknown to the pediatricians at the time. Eight years later we had the opportunity of seeing another child with symptoms of the same type.

In 1934, in the AMERICAN JOURNAL OF DISEASES OF CHILDREN, Dr. Cornelia de Lange [2] published a very interesting article on "congenital hypertrophy of the muscles, extrapyramidal motor disturbances and mental deficiency."

In the present article we give a full history of our two observations of this syndrome, with photographs.

OBSERVATION 1

On Oct. 5, 1925, Claire B., aged 10 months, was admitted to the Crèche of the Hospital des Enfants Malades for treatment for stationary weight and prolapse of the rectum (fig. 1). At birth, the baby was slightly premature, weighing less than 2,000 Gm. She was breast fed for three weeks and then given a cow's milk formula till she was 3 months old. Her growth was slow but regular. After the age of 3 months her weight remained almost stationary, although her diet was normal and she had no digestive trouble of any importance. Dr. Putin de Pontoise modified the diet several times and gave injections of salt plasma. Obtaining no result, he sent her to the aforementioned hospital for advice.

Both the father and the mother were normal and in good condition. They had another little girl, aged 9 years, who was in good condition. One baby died of convulsions at 6 weeks, and another girl, at 5 years. There was one miscarriage

1. Debré, Robert, and Semelaigne, G.: Nourrisson ayant l'aspect d'une myopathie pseudo-hypertrophique généralisée, Bull. Soc. de pédiat. de Paris **23**:542 (Nov. 17) 1925.

2. De Lange, Cornelia: Congenital Hypertrophy of Muscles, Extrapyramidal Motor Disturbances and Mental Deficiency: Clinical Entity, Am. J. Dis. Child. **48**:243 (Aug.) 1934.

of four months. There was nothing abnormal on the mother's side; she had ten brothers and sisters in good health. The father's family, on the contrary, had some defects. He had a brother and an aunt with congenital mental deficiency and disturbances of walking.

The baby's appearance was totally abnormal. Her weight and height were those of an infant a few weeks old (weight, 8 pounds [3,628.7 Gm.]; height, 21 inches [53.3 cm.]). She was unable to sit up and could move only slightly. She cried raucously at intervals. The forehead was wrinkled. The eyelids were swollen, hiding the eyeballs; the hair of the eyebrows was scarce. The nose was flat and the mouth half open, showing a much enlarged tongue. The limbs, especially the lower ones, were too short for the length of the body.

On closer examination, one was struck by the abnormal protuberance of the muscular masses of the calves, like balls under the skin, giving the impression of

Fig. 1 (case 1).—The facies.

extraordinary strength, in great contrast to the child's obvious weakness. Palpation gave the sensation of a false hypertrophy with a kind of fibrous consistence.

The phenomenon extended to every muscular mass of the body, but was especially prominent in the muscles of the calves, the anterior external muscles of the legs, the quadriceps extensor muscles, the gluteal muscles and the muscles of the soles, and, on the arms, in the epicondylic and the bracchial triceps and biceps muscles; it was less marked in the scapular muscles. The thenar and hypothenar muscles formed regular cushions on the palm.

The muscles of the neck and the sternocleidomastoid muscles were also involved. The masseters formed two balls, and the swelling of the eyelids was probably due to a hypertrophy of the orbicular muscles, and it is probable that the macroglossia was due to a similar condition.

No indication of an abnormal condition was given on further observation. The liver and spleen were slightly enlarged. The lungs and heart were normal. The baby drank without difficulty; the stools were normal. The temperature was

between 96 and 98.7 F. The tuberculin and Wassermann reactions were negative. Also the x-ray picture showed nothing of importance.

In fact, the most striking feature of this case was the general muscular hypertrophy which gave the child the appearance of a prize-fighter or athlete, in vivid contrast to the muscular debility; also notable were the arrest of growth, the absence of all psychomotor or intellectual development and the absence of coordination in the movements. Examination revealed nothing else, and no muscular hypertonia was observed. The child was removed from the hospital at his parents' wish and died a few months later.

Our attention had been much drawn to this syndrome, but we awaited another case in order to be able to study it more closely. A child with

Fig. 2 (case 1).—Athletic aspect of the lower limbs.

a similar appearance was admitted in October 1933, and the following description gives the observations made.

OBSERVATION 2

Odette C., aged 2, was examined because of considerable backwardness of the psychomotor development.[3]

There was nothing noticeable in the family. Both the father and the mother were in good health. There were two other children, aged 8 and 5, who were healthy. No children had died. None of the family had ever shown nervous disease.

The child was born in good condition after an uneventful pregnancy. She was breast fed for two months and later was given a cow's milk formula. No acute disease developed.

3. Debré, Robert, and Semelaigne, G.: Hypertrophie musculaire généralisée du petit enfant, Bull. Soc. de pédiat. de Paris **32**:699 (Dec.) 1934.

After the first few months physical and intellectual development seemed to be more or less stationary. The child had little appetite and had to be forced to take her food. She was sent to us by Dr. Leveque of Rosoy-en-Brie, who had given her different schedules without success.

She weighed 14 pounds and 2 ounces (6,406.9 Gm.) and measured 25 inches (63.5 cm.). We were immensely struck by the considerable development of all the muscular masses, giving the same athletic appearance as in the first case, but still more impressive on account of her otherwise emaciated condition. The skin was very thin and adipose tissue practically nonexistent. Examination showed a general hypertrophy of all the muscles of the body.

Very noticeable were the wrinkled forehead, the flat nose, the scarcity of hair on the eyebrows and on the scalp and the long eyelashes. The eyelids appeared

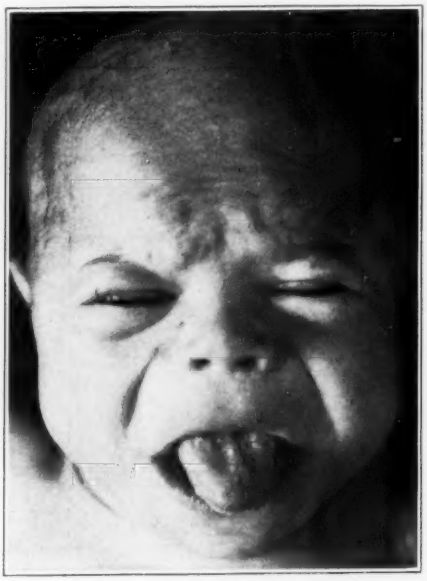

Fig. 3 (case 2).—The facies.

edematous and almost hid the eyeballs. The tongue was very large and contained in the mouth with difficulty owing to its size. The face had a fixed expression, almost the same as in congenital myxedema, but on closer examination it was observed that the swelling of the eyelids was due to an enlargement of the orbicular muscles and the macroglossia to hypertrophy of the muscles of the tongue. The temporal muscles, the muscles of the cheek bones and the masseters were also enlarged, causing this peculiar impression of the face. The child had no teeth. The neck was large and short, the muscles of the nape of the neck being overdeveloped. The arms were short, and the hands were thick, giving a false impression of fatness. The thenar muscles were overdeveloped. The forearms and upper part of the arms were thick, with the biceps and deltoid muscles particularly large.

The thorax and the pectoral muscles were also enlarged; the adductor and lateral muscles were protuberant. The spinalis dorsi showed a very noticeable cord.

The lower limbs were short in comparison with the trunk. The buttocks were prominent, making the waist appear slim. The thighs and legs were thick; the quadriceps femoris muscles and the muscles of the calves were especially hypertrophied. The feet were wide and short.

Deglutition was difficult and in phonation only inarticulate and raucous sounds were emitted, making it probable that both the tongue and the pharyngeal and laryngeal muscles were involved.

The smooth muscles did not appear involved. Roentgen examination of the digestive tract showed no trace of hypertrophic stenosis. The muscular strength was extremely small, the child being able to make only a few incoordinate movements.

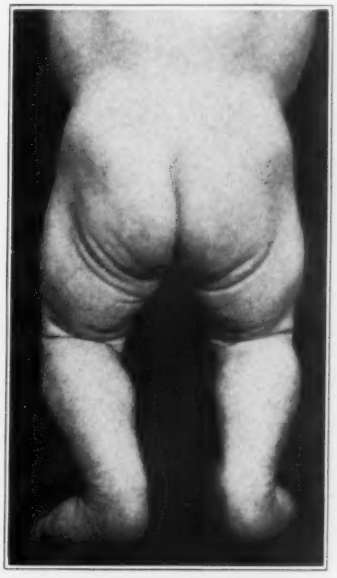

Fig. 4 (case 2).—Athletic aspect of the lower limbs.

There was pronounced muscular hypertonia; the limbs were stiff and difficult to bend or straighten. The stiffness was noticed by the mother, who found the child difficult to dress. This hypertonia was not accompanied by paroxysmal fits. The head was drawn backward, and the child was unable to stand or even remain in a sitting position.

The reflexes (patellar, front-tap and elbow) were feeble but present.

The integument was thin and dry, and panniculus adiposus was practically nonexistent.

The psychic development was almost nil. The child neither talked nor seemed to know her parents; she did not play or use her hands. She was fed automatically, showed no pleasure at the sight of food and did not try to hold her bottle. Deglutition was limited to fluids, of which she was unable to take a sufficient quantity. There was no increase in weight; in eighteen months the child gained only 1 Kg. On general examination there was observed only a slight mesosystolic murmur, which appeared to be extracardiac. The temperature was normal.

Roentgen examination (by Dr. Mignon) gave the following results: The thorax was wide and short with the normal transparence. The intercostal spaces at the base were wider than normal, giving rise to the opinion that the corresponding intercostal muscles were also enlarged. The diaphragm showed no anomaly of shape or contraction. The heart was slightly enlarged, with no anomaly in shape or beat. The mediastinum disclosed nothing of importance. The abdomen showed a large air pocket on the right side, almost in front of the liver. The gastric contraction was not sufficiently observed, the child being unable to retain enough of the bismuth. The blood chemistry (determined by Dr. Goiffon) showed normal

Fig. 5 (case 2).—Appearance of myxedema with muscular hypertrophy and hypertonia.

amounts of calcium (12 mg. per hundred cubic centimeters) and phosphorus (4.3 mg. per hundred cubic centimeters) and hyperlipemia (17.42 per cent total lipids).

In presenting our first case we suggested the very uncertain hypothesis of a generalized congenital hypertrophic myopathy,[4] but a closer study of our second case made us think of the possibility of a diagnosis of congenital thyroid insufficiency. The wrinkled forehead, flat nose, swollen eyelids, thick lips, large tongue and absence of hair on the eyebrows and scalp were all in favor of myxedema, as were the arrested growth and mental deficiency.

4. In such cases, the expression "pseudohypertrophy" is used in preference to "hypertrophy," as there is no such thing as hypertrophy of muscular fibers.

In spite of the condition of the skin, which in its thinness did not remind us of myxedema, we decided on a thyroid treatment, considering that the muscular hypertrophy might be the result of an overcharge of the muscles of a metabolic order and of neuro-endocrine origin.

The child was given each day, by mouth, 2 cg. of thyroid extract, this being the largest dose that she could tolerate.

The result was surprising. When we saw her again, six months later, she looked like a different baby. The muscular masses had decreased to nearly normal She had gained 2 Kg. in weight, and the aspect of a prize-fighter had disappeared

Fig. 6 (case 2).—The excellent results from thyroid treatment.

The facies was changed, and hair had grown on the eyebrows and scalp. The eyelids and tongue were normal in volume. Deglutition, from the fact of the decrease in the size of the tongue, was possible. Intellectual improvement was certain but slow. She recognized her parents and began to handle toys and play. Her crying was normal, but she had not yet begun to talk. Her movements were more rapid and precise, but she was still unable to sit or stand up. A remarkable fact was that the limbs had become supple and showed no muscular hypertonia.

The thyroid treatment was continued, and we examined the child again in October 1934. She had continued to improve in weight and height; the weight was 91.5 Kg.; she had gained in one year more than 4 Kg. and had grown 18 cm. Muscular hypertrophy and hypertonia had disappeared.

The child at 2 years had no teeth; at 3 years she had fifteen. Her psychomotor development was still very slow; she could laugh and play with her parents and toys but was still unable to talk, sit up or stand.

It was only after writing this history that we became acquainted with the article by Dr. de Lange. After study of that article and the photographs it appeared to us that the syndrome described by Dr. de Lange is very similar to the one that we observed in 1925 and 1933.

She reported four cases, three of which she had personally observed. The fourth was reported in 1889 (Bruck's case).

The first case was that of a boy, 2 months old, suffering from general hypertonia with opisthotonoid attitude and general muscular hypertrophy. He died when 3 months old. The postmortem observations were very interesting. We shall comment on them later.

The second case was that of a boy, 2½ months old, with athletic appearance, who had a short neck and showed general muscular hypertrophy. The skin was thick and hard, almost as in sclerema. He died when 3 months old.

The third case was that of a boy admitted to the hospital for fits of hypertonic contracture with opisthotonos and for permanent general stiffness. He had the typical facies, with large mouth, enlarged tongue, flat nose and sparse hair on the eyebrows and scalp and the general muscular hypertrophy giving an athletic appearance. The electrical reactions were normal. He died of bronchial pneumonia at the age of 5 months.

Bruck's case was that of a girl, 10 months old, suffering from respiratory disorders due to a tongue of such volume that part of it had to be excised to allow deglutition. There was general hypertrophy of the muscles giving the appearance of a prize-fighter. She died when 19 months of age.

Dr. de Lange was able to make a complete postmortem examination in the first of her cases. There were important lesions of the central nervous system, chiefly porencephalic lesions of the surface of the brain and underdevelopment of the corpus striatum. Without expressing a decided opinion as to the relationship between the cerebral lesions and the muscular disorders, she was convinced that these were more than a coincidence.

The different points of the syndrome were as follows: the congenital origin, the athletic appearance of a prize-fighter, the permanent and paroxysmal muscular hypertonia, the general muscular hypertrophy, the intellectual deficiency, the arrested development and the fatal prognosis.

Apart from the muscular hypertonia, this clinical picture is exactly similar to that in our first case. The history of our second case is exactly similar to that of the cases observed by Dr. de Lange, the boy in our case also showing permanent general hypertonia, less typical than in the children observed by Dr. de Lange, but certain. He alone lived, and certainly this was due to the thyroid treatment.

From the time that this treatment was instituted, the muscular masses decreased, the muscular hypertonia disappeared, the facies became nor-

mal, the weight and height began to increase and the psychomotor development started. Therefore under the influence of the thyroid treatment all the factors of the syndrome were modified, as well as the muscular hypertonia, whereas for eighteen months prior to the institution of this treatment no improvement had been noticed.

The success of the thyroid treatment seems to prove this case, as well as the first, to be one of congenital athyreosis. We were greatly mistaken in not diagnosing this in the first case, for muscular hypertrophy had already been described by Wieland in connection with that disorder. In Schlossman and Pfaundler's Handbuch he had already written:

Neben Hypotonie (Kassowitz, Siegert) der Muskulatur wird vielfach Hypertonie und Muskelsteifheit oft in Verbindung mit prall hervortretenden Muskelbäuchen beobachtet (Langhans, Friedjung, Pfaundler, Dieterle, eigene Beobachtungen). Die Reflexe, selten herabgesetzt und nicht immer leicht auslösbar, sind in den meisten Fällen deutlich gesteigert and zwar proportional dem Grade der Hypothyreose. Allgemeine Spastizität wie beim sog. Cretinisme nerveux McCarrisons in Indien gehört jedoch so wenig wie Herdsymptome seitens des Gehirns zum Krankheitsbilde der reinen Athyreose oder des hypothyreotischen Kretinismus (de Quervain). Die wahre Natur derartiger, geradezu als Kombination von Hypothyreose mit zerebraler Diplegie beschriebener Formen (Crookshank, u. a.) ist zur Zeit noch völlig ungeklärt. Immerhin halten wir auf Grund eigener, unveröffentlichter Beobachtungen von Kombination echter sporadischer Hypothyreose mit allgemeiner Spastizität, Verlust des Gehvermögens und stärkster Idiotie, auf welche die Schilddrüsenbehandlung ohne jeden Einfluss blieb, das Vorkommen einer selbständigen zerebralen Quote in vereinzelten Myxödemfällen auch beim Kinde für sehr wahrscheinlich.

[Besides hypotonia (Kassowitz, Siegert) of the musculature, hypertonia and muscular rigidity, often in connection with tautly prominent muscle bellies, are frequently observed (Langhans, Friedung, Pfaundler, Dieterle, own observations). The reflexes, rarely reduced and not always readily elicitable, are, in most cases, noticeably increased, proportional to the degree of hypothyreosis. General spasticity as in the so-called *cretinisme nerveux* of McCarrison in India belongs, however, just as little as the focal symptoms on the part of the brain to the symptomatology of pure athyreosis or of the hypothyreotic cretinism (de Quervain). The true nature of such forms that have been designated outright as a combination of hypothyreosis with cerebral diplegia (Crookshank and others) is as yet unexplained. At any rate, on the basis of our own unpublished observations on combinations of true sporadic hypothyreosis with general spasticity, loss of walking capacity and severest idiocy, in which the thyroid therapy was without any influence whatever, we consider the occurrence of an independent cerebral quota in rare cases of myxedema even in children as highly probable.]

The exaggerated development of the muscular masses, the athletic appearance and the absence of myxedematous infiltration explain our error in the first case but do not excuse it.

What comparisons can be made between Dr. de Lange's cases and ours?

Closer inspection of the histories and photographs in Dr. de Lange's cases leads us to believe that she has observed the same facts as we have. All the elements of the syndrome which she describes were found in ours. The mental deficiency and the arrested growth are the fundamental elements. Hypertrophy, or pseudohypertrophy, of the muscles was noted and could not have been more marked than in our cases, in which it made monstrosities of the children. General muscular hypertonia has been described by authors such as those named by Wieland as occurring frequently in congenital athyreosis. It is to this hypertonia that the bulging of the muscular masses is due.

The general spasticity was considered by de Quervain to represent a cerebral localization of the effects of athyreosis or hypothyroidism. This was very noticeable in our second case, impairing the active and passive movements of the limbs. The head was bent backward permanently. No paroxysmal fits or definite opisthotonos was noted, and in this lies the only clinical difference between our cases and those of Dr. de Lange. Is this really a fundamental difference or only a difference in the degree of hypertonia?

Again, on reading carefully the observations of Dr. de Lange,[5] we note that in her cases also there were symptoms of congenital athyroidism. The child in her case 3 showed a characteristic facies with wide mouth, enlarged tongue, wide nostrils, sparse hair on the eyebrows and scalp and thick, hard skin, giving the impression of a sclerema, as described in our case 2. The arrested growth was also noted in the child in case 3, who at 4 months was only 54 cm. long.

Nothing in the clinical picture allows us to put aside the thyroid origin of the syndrome. However, these different symptoms do not seem to have raised in the mind of Dr. de Lange, and at first not in ours, the possibility of congenital athyroidism; otherwise treatment would have been tried. It seems that success or failure of this treatment would alone have allowed one to place the cerebral lesions observed at autopsy in Dr. de Lange's first case and to know whether the general muscular hypertonia was due to an extrapyramidal syndrome with lesions of the gray nuclei of the central nervous system.

In our opinion, based on the rapid improvement and the disappearance of the general muscular hypertonia with the use of thyroid extract in one case, the cerebral lesions detected by our colleague in postmortem examination were only a coincidence. It is also known that it is not infrequent to find different cerebral lesions in congenital athyroidism. Success or failure of the thyroid treatment in similar cases in the future will alone solve the problem.

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5. We advise our readers to compare the photographs that accompany the two articles.

SUMMARY AND CONCLUSION

We report two cases of intellectual backwardness, arrested growth, retarded development and general muscular hypertrophy (athletic aspect), accompanied in one case with muscular hypertonia, in babies. The condition of the second baby was transformed by thyroid treatment. We claim that congenital athyroidism may cause this clinical syndrome and offer the idea that the histories of the cases observed by Dr. de Lange and described under the title "Congenital Hypertrophy of the Muscles, Extrapyramidal Motor Disorders and Mental Deficiency" pertain to the same category of syndromes. We advise, in such cases, systematic thyroid treatment, which may be of great advantage to the patient and may solve the question of the pathogenesis of the syndrome.

POLIOMYELITIS

II. THE BULBAR TYPE

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CLEVELAND

Elsewhere I have described the mechanism whereby the ordinary spinal type of poliomyelitis is produced.[1] The ordinary forms of monoplegia and paraplegia seen in human beings with this disease can be reproduced experimentally when the virus is introduced into an animal by way of the gastro-intestinal tract.[2] The spread in the latter instance is probably along the thoracolumbar outflow of the sympathetic system.[3] It has been pointed out likewise that there are good anatomic and physiologic reasons for believing that ordinary spinal poliomyelitis has its origin in the gastro-intestinal tract and that the virus spreads to the spinal cord along the sympathetic nervous system.[1] This hypothesis, which explains the production of this type of poliomyelitis, does not, however, explain the mechanism whereby bulbar poliomyelitis is produced.

Isolated nuclear paralysis of the ninth, tenth, eleventh or twelfth nerve is uncommon, but as the virus of poliomyelitis may travel along an axis-cylinder to a specific point, as it does in other nerves, it would be possible although not probable (except in cases of involvement of the seventh nerve) that a single nuclear lesion could be present. Granting, however, that the disease could be located solely in a single vagal nucleus (nucleus ambiguus), the maximum result of this unilateral involvement would be clinically minimal: One half of the soft palate would be flaccid, the voice would be nasal, and one vocal cord would be in the cadaveric position, but other than hoarseness and a falsetto voice there would be no change of note. There might not even be hoarseness and a falsetto voice. The important thing to remember in cases of unilateral lesions is that there is no marked dysphagia or dysarthria and that tachycardia and respiratory irregularities are rare. A unilateral nuclear or infra-

From the Department of Pediatrics, Western Reserve University, and the Division of Contagious Diseases, City Hospital.

1. Toomey, John A.: (*a*) An Explanation of the Mechanism of Infantile Paralysis Production in the Human Being, Ann. Int. Med. **8**:854, 1935; (*b*) Poliomyelitis, Jahrb. f. Kinderh. **143**:353, 1934.

2. Toomey, John A.: Spread of Poliomyelitis Virus from the Gastro-Intestinal Tract, Proc. Soc. Exper. Biol. & Med. **31**:680, 1934.

3. Toomey, John A.: Spread of Poliomyelitis Virus Along Nerve Fibers of the Sympathetic System, Proc. Soc. Exper. Biol. & Med. **31**:502, 1934.

nuclear lesion could not produce the symptoms observed in patients with bulbar poliomyelitis, nor could a unilateral break in the tract between the cortex and the nucleus ambiguus explain the syndrome, since such lesions are not clinically demonstrable because of the unbroken connection with the opposite cortical hemisphere. It would certainly stretch the imagination to suspect that the involvement was due to interruption of the corticobulbar tract simultaneous with a bilateral supranuclear or pseudobulbar lesion, although such a lesion is possible after the virus is injected intracerebrally or instilled intranasally into monkeys. It would presuppose nicely placed bilateral pathologic conditions, which is rather illogical; but even granting the possibility, clinical evidence does not support it. The objective findings in a case of bulbar poliomyelitis are not those of complete involvement, as in a case of typical bulbar lesions, since in the former the masticating muscles are not usually affected, the mouth can be opened against resistance, the teeth can be clenched together, the jaw can be protruded and food does not fall out of the oral cavity.

If these lesions were caused primarily by involvement of the nuclei bilaterally, they would represent an unusual anatomic fortuity for the virus of poliomyelitis or for any kind of virus, and in explanation one would have to suppose the presence of local areas of lessened resistance or areas of specific sensitivity, a somewhat overworked theory that is used to explain why the lumbar portion of the spinal cord is usually first involved in cases of this disease.

From the previous considerations and from those which follow it is obvious that most cases of bulbar poliomyelitis are really cases of primary involvement of the vagus and its nerve motor nuclei.

To understand my hypothesis it is necessary to realize that the virus has an obligate affinity for gray nerve fibers. Injection of the virus about a myelinated nerve causes no reaction,[4] but when a myelinated nerve is injured by crushing with a hemostat and the virus is injected directly into the nerve so that it approximates the gray-fibered axis-cylinders the disease may be produced.[5] The places in the body from which virus is absorbed are those in which there are plenty of gray fibers, such as the intradermal area,[6] the eyeball,[7] various nerves,[8] the

4. Toomey, John A.: Unpublished experiments.

5. Fairbrother, R. W., and Hurst, E. W.: The Pathogenesis of, and Propagation of the Virus in, Experimental Poliomyelitis, J. Path. & Bact. **33**:17, 1930. Hurst, E. W.: A Further Contribution to the Pathogenesis of Experimental Poliomyelitis: Inoculation into the Sciatic Nerve, ibid. **33**:1133, 1930. Toomey.[2]

6. Brodie, M., in Poliomyelitis: A Survey Made Possible by a Grant from the International Committee for the Study of Poliomyelitis, Baltimore, Williams & Wilkins Company, 1932.

(Footnotes continued on next page)

olfactory nerve,[9] the peritoneum [10] and the cerebral area.[11] It is also necessary to realize that in addition to an area of absorbing gray fibers there must be a fairly direct connection with the central nervous system. Thus, the disease is invariably produced by the intracerebral injection and by the intranasal instillation of small doses of virus in suspension, but thousands of these same dosage units are required to produce the disease when the injection is made intracutaneously. After it is prepared any myelin-sheathed somatic nerve can be employed to carry the virus, and the rapidity with which the disease appears after the injection depends on the nearness of the connecting curve to the lumbar area. Thus there is no reason why any nerve, including the vagus nerve and the chorea tympani, cannot naturally carry the virus if the end-fibers come in contact with it.

The clinical findings bear directly on this question. In 12 of the 71 cases studied by Draper, Peabody and Dochez [12] and in 42 of the 685 cases described by Wickman [13] combined spinal and bulbar disease was noted. Of 431 patients admitted to the department for contagious diseases of the City Hospital, 68 could be said to have had the bulbar type of involvement. These patients, however, can be divided into two well defined groups: group 1, those who had symptoms referable to the vagus nerve first and only later had involvement of other cranial nerves, and, group 2, those who had involvement of the seventh nerve first, only occasionally showing extension to the other nerves of the bulb. In the former group there were 45 patients, 26 of whom died; on 11 autopsy was performed. In the latter group there were 23 patients, only 2 of whom died. The latter group will be reported on later, as the mechanism for the production of the disease in them is totally different from that in the former group. Fifteen patients of the

7. Landsteiner, K., and Levaditi, C.: La transmission de la paralysie infantile aux singes, Compt. rend. Soc. de biol. **67**:592 and 787, 1909.

8. Demme, H.: Ueber experimentelle Poliomyelitis, Deutsche Ztschr. f. Nervenh. **116**:156, 1930.

9. Flexner, S., and Lewis, P. A.: Experimental Epidemic Poliomyelitis in Monkeys: Characteristic Alterations of the Cerebrospinal Fluid and Its Early Infectivity; Infection from Human Mesenteric Lymph Node, J. A. M. A. **54**:1140 (April 2) 1910.

10. Landsteiner, K., and Popper, E.: Mikroskopische Präparate von einen menschlichen und zwei Affenrückenmarken, Wien. klin. Wchnschr. **21**:1830, 1908.

11. Flexner, S., and Lewis, P. A.: The Transmission of Acute Poliomyelitis to Monkeys, J. A. M. A. **53**:1639 (Nov. 13) 1909.

12. Peabody, F. W.; Draper, G., and Dochez, A. R.: Clinical Study of Acute Poliomyelitis, Monograph 4, Rockefeller Institute for Medical Research, 1912.

13. Wickman, I.: Acute Poliomyelitis (Heine-Medin Disease), translated by W. J. M. A. Maloney, Nervous and Mental Disease Monograph 16, Washington, D. C., Nervous and Mental Disease Publishing Company, 1913.

first group had constipation so intractable that even the parents were aware of the difficulty. Fourteen had severe headache. Eleven suffered from nausea and 26 from vomiting that was both frequent and distressing. Thirty-six of the 45 patients had dysarthria and dysphagia, and 22 had aphonia. Thirty-eight had obvious involvement of the muscles of the palate. Probably all of them had paralysis of the palate, with dysarthria and dysphagia, but on account of the condition of the patient at the time of his admission to the hospital it was often impossible to acquire information as to the status of the muscles of the throat. With this fact in mind the findings were striking and served to focus attention on the vagus nerve.

In further analysis of the data it was found that in 21 of the 45 patients there was involvement of the tenth nerve alone or in conjunction with involvement of some other cranial nerve or nerves. Thirteen of the 45 patients had paralysis of the arms, in addition to palsy of the vagus nerve, and it was interesting to note that the paralysis of the arm occurred secondarily. Two patients later had involvement of the legs, while in 1 patient the legs and then the thorax were involved. In 10 patients the legs became paralyzed first after symptoms of bulbar involvement appeared; in 3 of these the arms were involved later, in 2 the arms and thorax, and in 1 the thorax. As can be seen in the following tabulation, 16 of the 26 deaths occurred during the first week:

Day of disease	2	3	4	5	6	7	8	10 to 20	21 to 25
Deaths	3	3	4	1	3	2	3	4	3
	16						10		

In the cases in which death occurred there were some curious clinical observations on involvement of the cranial nerves. The third nerve was involved in 1 case; the seventh nerve, in 9; the eleventh nerve, in 3 (?), and the twelfth nerve, in 3 (?). Undoubtedly other cases would have been found in which there was involvement of the ninth, tenth and twelfth nerves had the condition of the patient warranted more detailed examination. In 1 case there was absence of pupillary accommodation, with ptosis of the left lid. In another, the right pupil was larger than the left. In 1, there was a crossed palsy of the facial nerve and in 2 cases the paralysis started in the seventh nerve and went on to involvement of the sixth and tenth nerves.

Nineteen of the 45 patients with the bulbar type of poliomyelitis recovered. An interval of from two to six days usually elapsed between the time when the patient first became ill and the time when he was admitted to the hospital. The shortest period after which the patient could swallow comfortably was six days after admission to the hospital; the longest, eighteen, and the average, nine and five-tenths. In 1 case

the fifth nerve was involved; in 1, the sixth nerve; in 3, the seventh nerve; in 2, the ninth nerve; in 4, the eleventh nerve, and in 1, the twelfth nerve. In 1 case the right pupil was larger than the left, with ptosis of the right lid and conjugate deviation to the left. Combined involvement of cranial nerves was slight save in 1 case, in which the fifth, seventh, ninth, tenth and eleventh nerves were involved. In 1 case there was conjugate deviation to the left, as well as inability to converge the eyeballs, with paralysis of both feet and legs.

The objective findings in these cases indicated involvement of the vagus nerve, but an account of the symptoms pointed more clearly to its primary involvement. A few of the histories illustrate the unvarying and typical sequential occurrence of symptoms.

G. E. L., a boy 11 years of age, was admitted to the hospital on September 6, the fifth day after the appearance of symptoms. On the first day of the illness the child had a "big head," headache and pain in the face. A diagnosis of sinusitis was made. At this time the patient had intractable constipation. On the second day there were slight but barely noticeable blurring of speech and difficulty in swallowing. On the third day all the previous findings were aggravated. On the fourth day the patient had stiff neck, headache and complete paralysis of the left arm. On the fifth day, the day the patient was admitted to the hospital, there were dysphagia, dysarthria, aphonia, paralysis of the muscles of the palate, stiff neck, pain along the spine, paralysis of the left arm, loss of the gag reflex, positive Kernig and Brudzinski reflexes and absence of the superficial abdominal reflexes. The spinal fluid cell count was 80, with 81 per cent mononuclear cells and a 4 plus reaction to the Pandy test. On the sixth day, soon after midnight, the temperature began to rise, the pulse rate could not be counted, the respiratory rate dropped, the patient became unconscious and marked cyanosis and anoxemia without dyspnea developed. Death occurred ten hours later.

A. K., a boy 13 years of age, was admitted to the hospital on August 11, the eighth day of the disease. On the first day of the illness he had diarrhea, cramps and headache. On the second day he had pain in the back of the neck. On the third day he was nauseated and vomited frequently, and the headache was more severe. The fourth day he complained that his throat bothered him, and the mucus was profuse. He gradually became worse on the fifth, sixth and seventh days. On the eighth day he became delirious and could neither speak nor swallow. On admission to the hospital on the afternoon of the eighth day the patient was stuporous but could be aroused. There were dysarthria, dysphagia, aphonia, paralysis of the muscles of the palate, rigidity of the neck, pain in the back, absence of abdominal and deep body reflexes, a positive Kernig sign and athetoid movements of the left leg. The patient was markedly dehydrated, and mucus drooled from the mouth. The spinal fluid contained 65 cells, all of which were mononuclears, and the reaction to Pandy's test was positive. The temperature began to rise twelve hours after the patient was admitted to the hospital; he became tensely cyanotic; respirations were labored, slow and irregular, and tachycardia and convulsions set in. Death occurred seven hours later.

J. G., a boy 9 years of age, was admitted to the hospital August 30 and was discharged on September 20. On the first day of illness he had fever, and a

diagnosis of sore throat was made. On the second day the condition was about the same, and on the third and fourth days the child's arms and legs hurt. On the fifth day a diagnosis of diphtheria was made and the child was sent to the hospital for an intubation. At the time of his admission to the hospital there were weakness of the triceps muscle of the left arm, paralysis of the soft palate and uvula, dysarthria, dysphagia, aphonia and occasionally bradycardia. There was still sensation about the external auditory canal. On the sixteenth day in the hospital the patient was able to swallow and to speak fairly accurately. By the twenty-seventh day, the day of discharge, power had returned to the triceps muscle and dysphagia and dysarthria were not present, but speech was still a little aphonic.

P. P., a boy 8 years of age, was admitted to the hospital on September 24 and was discharged on November 19. On September 19, the first day of illness, the child was nauseated and had anorexia; nevertheless he went to school. His mother noticed at night that his finger-nails were as blue as indigo and that he breathed "funny." On the third day the child had difficulty in swallowing. On the fourth day he could not eat, breathing was irregular and his voice was furred. On the fifth day these conditions were aggravated, and on the sixth day the patient was admitted to the hospital with a diagnosis of diphtheria requiring intubation. On admission to the hospital there were dysphagia, dysarthria and aphonia, irregular breathing and an erratic pulse rate. The patient was markedly constipated. Mucus was present in the mouth and throat. Postural drainage was instituted, and aspiration from the mouth and throat was started. On the seventh day the aspirator no longer bothered the patient, because there was no sensation in the throat, although it was present around the external auditory meatus. The patient had periods of delirium on this day and on the eighth and ninth day. On the tenth day he could gag, and on the nineteenth day the muscles of the palate had nearly regained their tone.

When the clinical symptoms in these patients with bulbar poliomyelitis are analyzed and tabulated in chronological order as they occurred, the first symptom to be noticed was nausea accompanied by vomiting so severe at times that neither water nor food could be tolerated; in some cases nausea was present and not vomiting, and vice versa. Many patients were unable to give information about their symptoms, and the fact that it is not possible to report more instances of nausea and vomiting does not mean that these symptoms were not present. The point to be considered here is not the number of patients who had this and that symptom but the sequential occurrence of those symptoms that were present. Nausea and vomiting could be caused by a central irritation of the vagus nerve, but they could just as well be attributed to peripheral involvement as a result of stimulation of the end-fibers of the vagus nerve of the gastro-intestinal tract. One need not predicate central irritation of the vagus nerve in acute inflammatory conditions of the abdomen requiring surgical intervention, nor is it any more logical to assume that the early symptoms of this disease are of central origin. Frequently pain was felt in the epigastrium.

From one to three days elapsed between the time the first gastro-intestinal symptom and pain were noted and the beginning of paresis of the laryngeal and pharyngeal muscles. So gradual is the onset of weakness of the muscles of the throat that the condition often is not noted until dysphagia is nearly complete and dysarthria and aphonia have set in. Rarely is the patient admitted to the hospital before frank paralysis of the muscles of the throat has occurred, although I have been fortunate enough to observe its development in 2 cases. In both instances, after the gastro-intestinal pain and vomiting appeared, each patient began to have peculiar respiration and irregularities of the pulse beat. Periods of hyperpnea occurred and also periods of a slowed respiratory rate with widened amplitude of depth and periods of hyperpnea with shallow respirations alternating irregularly with an occasional deep, full inspiration; but at no time was there a period of complete apnea. In neither of these cases, either at this stage or when the muscles of the throat were first involved, was there any cyanosis. The pulse was erratic, alternating in irregularity between obvious bradycardia and tachycardia.

Nearly all the patients were admitted to the hospital because of dysarthria, dysphagia and aphonia. Most of them were sent to have intubation or a tracheotomy carried out for diphtheria. If there is an upward spread of the virus along the vagus nerve from the gastro-intestinal tract, the nucleus to be reached first would be the nucleus ambiguus, after which the recurrent laryngeal nerves would become involved to an extent depending on the amount of damage to the nuclei. Unfortunately it was not possible to observe the reactions of each patient on admission to the hospital, since the patient usually was unconscious, but in 4 cases it was noted that in a variable time later, a matter of hours, the patient began to lose sensation in the pharynx and the aspirator employed to remove the mucus no longer irritated the posterior pharyngeal wall. This would indicate a spread of the virus to the dorsal vagal nuclei. In 2 cases the spread stopped here, and sensation returned in three days. The majority of the patients died shortly after the laryngeal and pharyngeal muscles were paralyzed or after the pharynx had become insensitive and before other cranial nuclei were involved by extension, usually drowning in their own secretions or suffocating because the phrenic center in the cervical area had also become involved, a fact which clearly explains why in so many cases of so-called bulbar poliomyelitis there is a lack of corroborative histopathologic changes.

When the lesion has become massive in the dorsal vagal nuclei the patient usually becomes moribund. The clinical evidence that this area is involved is found in the character of the pulse and the respiratory

rate and, to a less extent perhaps, the curve for temperature, since ungovernable tachycardia results (vagus escapement), coupled with a curious slowing of the respiratory rate with marked cyanosis, anoxemia and high temperature. There is no apparent air hunger, although there is anoxemia that cannot be appreciated by the patient because of the central involvement. If the patient is not unconscious at this time he soon becomes so, and death occurs ordinarily within from twelve to twenty-four hours. In my series only 1 patient who exhibited symptoms of vagus escapement lived. In cases of vagus escapement, and they are only few of the many cases of bulbar poliomyelitis, there is enough histopathologic evidence to support the microscopic diagnosis of bulbar poliomyelitis. All the other cases of bulbar poliomyelitis are merely cases of bilateral involvement of the vagus motor nuclei in patients who usually die long before the virus has reached the dorsal vagal nuclei and other cranial nerves.

One can easily understand why paralysis of the ocular muscles should occur, since the very position of their nuclei tends to include them in any process that would spread upward in the gray matter of the medulla and pons. Paralysis of lateral conjugate movements and of convergence is often the result of a large pontile lesion which involves the posterior longitudinal bundle. Fibers run from the bundle to the nuclei of the muscles of the eye and to the opposite bundle and ordinarily might become involved in an inflammatory lesion of the contiguous gray matter. Theoretically, if only the bundle and the nucleus ambiguus are involved and the process stops spreading at this point, recovery from paralytic conjugate deviations and inability to converge should be prompt and complete, as was illustrated in the following case:

M. M. S., a girl 4½ years old, became ill on October 24 with fever, malaise and anorexia. On October 25 she had pain in the stomach and vomited. On October 26 she cried all day, suffering from pain in the stomach and obstinate constipation. On October 27 she had pain in both legs. That night there was paresis of the legs. On October 28 she was unable to stand. On October 29 she was admitted to the hospital. At this time the symptoms included drooping of the left eyelid, failure of conjugate deviation to the right and paresis of both extremities, deviation of the tongue to the right and some difficulty in swallowing. On October 30 the child had convulsions and both legs became paralyzed. On November 3 the function of both legs had returned, and there was no difficulty in swallowing. On November 4 there was paralysis of the right lateral rectus muscle but no failure of conjugate deviation. On November 13 the external rectus muscle had regained its function.

The ptosis of the lid that is occasionally noted may be the result of a lesion of the oculomotor nucleus. Frequently, however, the lid can be raised with ease. This would denote paralysis of the superior tarsal muscle, supplied by sympathetic nerve fibers. Occasionally temporary

dilatation of the pupil is seen in the ordinary spinal type as well as in the bulbar type of poliomyelitis. Here again the physical signs do not necessarily indicate paralysis of the oculomotor nucleus but rather point to a stimulation of the ciliospinal center of the spinal cord.

Some authors have claimed that poliomyelitis spreads along the olfactory nerve to the bulb and have referred to injections into animals and the results obtained at autopsy on human subjects.

Histologic sections of material taken from monkeys into which poliomyelitis virus has been injected intracerebrally and intrasciatically are interesting, but they prove nothing more than what happens in animals into which the virus is injected through a highly artificial portal of entry. Without definite knowledge as to the portal of entry, such histologic evidence merely indicates trends and tendencies; no *ex cathedra* conclusions can be drawn that would controvert obvious and material clinical facts.

The autopsy observations of Rissler [14] (3 cases) and of Wickman [13] (14 cases) are often referred to, but the most quoted report is that of Harbitz and Scheel.[15] When the observations of the latter are examined it is noted that the very data that they presented is much more in favor of a gastro-intestinal than of any other portal of entry. In this connection it is interesting to note that Harbitz and Scheel thought likewise originally. Records of autopsy observations on 19 cases were included in their monograph. Two of the patients suffered from encephalitis, and 4 died after the acute stage of the disease had passed. It is obvious that the observations on these 6 cases give little light on the portal of entry and method of spread of poliomyelitis. Only 13 died during the acute stage of the disease, in 6 of which complete autopsy was performed, in 7 partial autopsy limited to the nervous system and in 1 no medullary section. Four patients were female, and 9 were male, and the ages ranged from 2½ to 38 years. In no case was the clinical information obtained at first hand, nor was the patient cared for by the authors in any instance.

In Harbitz and Scheel's microscopic observations the pia was found to be most inflamed over the lumbar and cervical enlargements. Except in their cases 3, 9 and 12, the inflammation of the cord was most severe in the lumbar enlargement, and except in cases 3 and 10 the next most involved area of the cord was the cervical area. Ignoring the first thoracic segment, except in cases 3 and 10, it was found that the thoracic

14. Rissler, J.: Zur Kenntnis der Veränderungen des Nervensystems bei Poliomyelitis anterior acuta, Nord. med. ark. **20**:22, 1888.

15. Harbitz, F., and Scheel, O.: Akute Poliomyelitis und verwandte Krankheiten: Pathologisch-Anatomische Untersuchungen aus den Epidemien in Norwegen, 1903-1906, Norsk mag. f. lægevidensk. **68**:1145, 1907.

segments always had the least involvement. I have particularly called attention to the spotty spread of the disease in man and have been able to give an anatomic explanation for this anomaly that is not possible with any theory of absorption and spread by means of the olfactory nerve.[1a]

In Harbitz and Scheel's cases the areas of gray fibers and the vessels in the pons were always involved. The patients in cases 2, 5, 7, 9, 12 and 13 probably died of respiratory failure due to paralysis of the phrenic nerve before symptoms of involvement of the vagus nerve occurred. In all the remaining cases, except in case 4, in which there was some doubt, there were signs of involvement of the vagus nerve in the presence of dysarthria, dysphagia, etc., and in all the cases there was enough involvement of the cranial nerves in the brain stem to have evinced symptoms if the patient had lived longer. The symptomatology of the illness is not complete, perhaps because the authors thought in terms of a general infection with special localizations and not in terms of anatomic spread up the vagus nerve coincident with a spread along the thoracolumbar outflow to the lumbar and cervical enlargements.

In 9 cases the condition started as spinal poliomyelitis and ended with involvement of either the cervical area or the bulb. In cases 7, 10, 12 and 13 the condition was listed as a pure bulbar lesion by Harbitz and Scheel. I agree that in these cases the condition started and ended with diffuse bulbar involvement, but in case 13 it seems to have been initiated in the area of the cervical portion of the spine and to have ended suddenly with involvement of the phrenic area or the bulb. It is curious that in this case the inflammation of the cord substance was most marked in the lumbar area.

Although the histories are scanty and were reviewed at second hand, the patients nevertheless showed symptoms of involvement of the vagus nerve, as evidenced by aphonia, dysphagia and dysarthria in 8 of the 13 cases. Five of the patients died probably before symptoms had become obvious. There was utter lack of evidence of other cranial involvement save in case 4, in spite of the fact that even the pathologic picture seemed to show infiltration of the nuclei.

Autopsy may show bulbar involvement in patients who had no symptoms, but in the cases reported by Harbitz and Scheel, as in the cases I have observed, there was probably phrenic involvement before symptoms could have occurred or involvement of the substantia reticularis so sudden that the vital centers were poisoned. Cases have been referred to in which symptoms of bulbar involvement have occurred without evidence in the bulbar area at autopsy. This is not illogical if one assumes that the virus in passing along the vagus nerve may be virulent enough to poison the recurrent laryngeal nerves on the way to the bulb. In such a case the patient would die because he would be

drowned in his own secretions before the virus had time to reach the bulb. This assumption, however, would presuppose that the virus may irritate the nerve axon in passage. The virus or whatever combination of influences brings about the disease in man might cause immediate paralysis of the axons. However, no positive and conclusive evidence has been offered on this point. In the experimental animal the virus that has been obtained from the spinal cords of monkeys has not proved to be destructive for axons. Dyspnea and other symptoms that arise as a result of the paralysis of thoracic and phrenic muscles may be confused with comparable symptoms seen in cases of bulbar paralysis.

The following history of a case and the record of observations at autopsy will illustrate my own findings:

P. K., a boy 9 years of age, had malaise on September 17. He also spoke thickly. On September 18 he stayed at home from school because he continued to be tired and could not swallow and his speech had become furred. On September 19 he was definitely worse; he could neither speak nor swallow and he "frothed at the mouth!" On September 20, two hours before he was admitted to the hospital, he began to gasp for breath and became cyanotic; the respiratory rate became retarded, and the pulse rate was fast. On admission to the hospital there was bilateral involvement of the muscles of the palate; the patient could neither speak nor swallow, and the pharynx was filled with mucus. He could open his mouth and stick out his tongue. No other involvement was found save that referable to the tenth nerve. He died suddenly fifty minutes after he was admitted to the hospital, the heart stopping first and the breathing continuing somewhat irregularly for about two minutes. There was no involvement of the extremities. From the symptoms it was thought that the nuclei ambigui and the dorsal vagal nuclei were involved.

Postmortem examination was carried out two hours and ten minutes after death. Grossly there were some dilatation of the vessels of the cortical pia-arachnoid and hyperemia of the subarachnoid area of the cord. Examination of cut sections gave grossly negative results. Microscopically the cerebral cortex, the lenticulostriate area and the thalamus showed some hyperemia but no perivascular infiltration or cellular destruction. In the pons the same condition was noted that was present in the medullary area, but the polymorphonuclear cells were more numerous. There was obvious destruction of nerve cells. In the posterior medullary area the vessels were hyperemic and had an extensive cuffing of small and large mononuclear cells, with a few polymorphonuclear and plasma cells. There were definite cytoplasmic granulation of the nerve cells and only moderate infiltration of the gray and white matter, with small and large mononuclear cells and polymorphonuclear leukocytes.

The nuclei ambigui and the dorsal vagal nuclei were involved bilaterally, the left nucleus ambiguus showing almost complete necrosis.

The usual picture of perivascular cuffing and involvement of the anterior horn cells was found in the cervical and lumbar area of the cord. However, there was not the destruction present here that was seen in the medullary area.

If one assumes, then, that the virus has almost an obligate affinity for gray fibers and when taken up by the gray-fibered axons travels encased in a medullated nerve only to spill over and in a bizarre fashion

to involve contiguous territory of unmyelinated character when the nerve loses its myelin sheath, then one has the explanation of events in the case of so-called bulbar poliomyelitis. The bulbar area may be involved alone, but since the gray end-fibers of the thoracolumbar outflow also absorb the virus, there is usually a pathologic reaction in the cord even though symptoms of paralysis may not as yet have appeared in the muscles of the extremity. The clinical picture of bulbar poliomyelitis can best be understood by assuming that the portal of entry is through the gastro-intestinal tract.

Experiments confirm this hypothesis, for when the virus is injected into the vagus nerve on the right side the clinical condition of bulbar palsy is produced in the Macacus rhesus monkey, with dysarthria and dysphagia, and the histopathologic picture is similar to that present in a human being with bulbar poliomyelitis.[16]

CONCLUSION

Clinical observations indicate that the virus of poliomyelitis in a certain percentage of cases spreads up both the vagus nerves from the gastro-intestinal tract to involve the vagal motor nuclei and, by contiguous extension, other cranial nuclei.

16. Toomey, John A.: Experimental Production of Bulbar Poliomyelitis, Proc. Soc. Exper. Biol. & Med. **32**:628, 1935.

ASTHMA IN CHILDREN

XII. INFLUENCE OF SPECIFIC AND NONSPECIFIC TREATMENT ON THE DIFFERENTIAL LEUKOCYTE COUNT, WITH SPECIAL REFERENCE TO THE EOSINOPHILS

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The rationale of specific "desensitization" treatment as now employed for the relief of hay fever and asthma is based on the premise that the injection of specific antigen causes a diminution of its specific antibody in the host with resultant actual hyposensitization and increased tolerance for the offending substance (antigen). On the other hand, many workers hold that nonspecific agents exercise their power by altering the reactivity of the whole organism through stimulation of cells. Both forms of therapy—specific and nonspecific—possibly exert their influence through the sympathetic nervous system. The beneficial effects resulting from treatment with specific antigens are generally conceded to be more prompt and lasting than those obtained with nonspecific antigens. Nevertheless, the occurrence of certain complications in patients with allergic diseases frequently is an indication for supplementary nonspecific therapy. The administration of both forms of therapy usually involves the introduction of foreign protein into the tissues.

It is well known from experiments on animals that the injection of foreign protein causes a rise of the eosinophil cells in the blood plasma and tissues. Eosinophilia is met with in a variety of conditions, but it is generally agreed that the eosinophil is in some way bound up with the allergic syndrome. Little is yet known concerning the nature and function of the eosinophils. The chief function probably consists in bringing about the disintegration and removal of foreign protein from the tissues.

In view of the foregoing remarks and of the enormous number of injections of foreign protein administered annually to allergic persons, it was believed that a detailed study involving the influence of specific and nonspecific therapy on the differential leukocyte count with special reference to the eosinophils (eosinophilic index) was warranted. It was further thought that more information could be obtained from a small series of cases with a larger number of differential counts than from a large series of cases with a smaller number of counts.

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The present study was carried out on thirty-eight ambulant patients in the clinic ranging in age from 2½ to 15 years. Six patients had hay fever, and the remainder had asthma with or without hay fever. The total number of differential leukocyte counts was nine hundred and seventy-one, or an average of twenty-five per patient.

In the children with asthma not based on pollen allergy the condition was of the chronic type and refractory to the accepted standards of modern treatment. The positive reactors (to cutaneous tests) prior to the present study have for varying periods of time been placed on restrictions according to the individual sensitivity. These restrictions were continued through this investigation.

For convenience of presentation the patients comprising this study were divided into two groups: (1) those given injections of nonspecific agents and (2) those given injections of pollen antigens.

NONSPECIFIC AGENTS

A large number of biologic substances, colloidal metals and certain drugs have been used to produce nonspecific reactions for their therapeutic effect. In adults many of these measures are employed with the view of inducing a systemic or general reaction, much attention being focused on the chill, fever and the white cell count. However, in children a general reaction following a nonspecific treatment is not desirable or commonly practiced because of the risk of overstimulating a labile autonomic nervous system, with resultant aggravation of symptoms. General reactions following the dosage of nonspecific agents (venom [crotalin] protein solution and sterilized milk) employed in our series of cases were not encountered.

The venom protein solution (Crotalus horridus) employed in the beginning of this study was furnished by Dr. R. H. Spangler of Philadelphia. The subsequent venom solution was prepared by us from evaporated, dried, yellowish crystals of Crotalus atrox. The extracting fluid consisted of equal parts of sterile water and glycerin. The solution was prepared so that 1 cc. represented 1.2 mg. (1/50 grain) of the dried crystals and was examined for aerobic and anaerobic bacteria before being used. The extract was not passed through a Seitz or Berkefeld filter and was freshly prepared every month.

The milk antigen was prepared as follows: Skimmed milk was placed in shallow pans and exposed to the air for some hours for the purpose of obtaining a high bacterial count, after which it was sterilized by heat in an autoclave for one-half hour under a pressure of 20 pounds (9.1 Kg.) and then tested for sterility. Phenol of a concentration up to 0.5 per cent was added. This milk antigen was freshly prepared every three weeks, though subsequent experience has shown that under proper refrigeration its sterility was maintained for at least three months. This

nonspecific agent served as a double antigen—milk proteins reenforced with bacteria. None of the patients given injections of milk exhibited a clinical intolerance or a positive cutaneous reaction to milk.

VENOM (CROTALIN) PROTEIN SOLUTION

Spangler [1a] in a period of more than twenty years employed venom (crotalin) protein solution with beneficial results in the treatment of epilepsy in thousands of instances and also in some patients with migraine, asthma and hay fever.[1b] Venom protein solution contains a peptone and a globulin [2] and a proteose enzyme [3] and is physiologically standardized by the reptile itself. Newman [4] reported that only the globulin element lengthened the clotting time of the blood and increased the permeability of the walls of the blood vessels.

Spangler contended that crotalin protein solution met every requirement chemically and physiologically, and it therefore appeared to him to be a satisfactory agent to produce nonspecific resistance for therapeutic purposes. He found that no general leukocytosis was produced following the injection of venom protein. On comparing the total leukocyte counts before and after injection a slight leukopenia was found to occur within the first twelve hours, and by thirty-six hours or sooner the total number of white cells returned to about the level at which it was before injection. An increase in the number of erythrocytes occurred in from twelve to thirty-six hours after the injection. Of particular interest were the proportional increase in the percentage of the eosinophil cells and a decrease in the polymorphonuclear neutrophils in the differential count.

The patients in this series were given injections (intramuscular) of venom protein solution, usually at weekly intervals, and since the eosinophil is the cell under particular study attention was focused on the differential leukocyte count. All the cells revealed in the differential leukocyte count were noted, but only the polymorphonuclear neutrophils, lymphocytes and the eosinophils are recorded, because the remaining cellular elements did not prove to be of any significance.

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1. Spangler, R. H.: (*a*) New York M. J. **98**:651 (Oct. 4) 1913; **104**:531 (Sept. 16) 1916; **107**:727 (April 20) 1918; M. J. & Rec. **120**:495 (Nov. 19) 1924; **122**:313 (Sept. 16) 1925; (*b*) Nonspecific Desensitization Therapy in Allergic Asthma; the Eosinophilic Index as a Guide to Intramuscular Injection of Venom Protein, with Case Report, Arch. Int. Med. **36**:779 (Dec.) 1925.

2. Mitchell, S. W., and Stewart, A. H.: A Contribution to the Study of the Action of the Venom of the Crotalus Adamanteus upon the Blood, Tr. Coll. Physicians, Philadelphia **19**:105, 1897.

3. Flexner, S., and Noguchi, H.: Snake Venom in Relation to Hemolysis, Bacteriolysis and Toxicity, J. Exper. Med. **6**:277 (Sept.) 1903.

4. Newman, quoted by Spangler, R. H.: M. J. & Rec. **120**:495 (Nov. 19) 1924.

Eleven children with bronchial asthma (ten with positive reactions and one who had a negative cutaneous reaction) were given injections of venom protein solution. The pertinent findings in each case are set forth as follows:

CASE 1.—I. T., a boy, was 3 years of age at the onset of asthma. He came under observation at 4 years of age, when attacks of asthma occurred almost daily. Skin tests revealed many positive reactions, with clinical intolerance to the cereal grain group and to egg.

In 1928, twenty-three injections of venom protein solution were given, the maximum dose being 0.45 mg. (1/150 grain). Sixty-seven differential leukocyte counts were made over a period of one hundred and fifty days (chart 1). Prior to the initial injection of 0.1 mg. (1/600 grain) of crotalin the eosinophil count was 15 per cent.

During the first seven weeks of treatment no definite relief from asthma was noted, and in most instances after the injection of crotalin only a slight rise in the number of eosinophils occurred. In the second week of April the patient's two

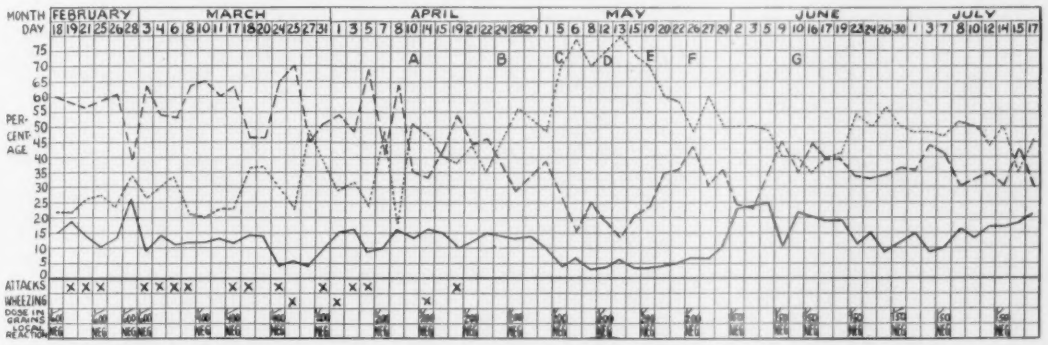

Chart 1 (case 1).—Differential leukocyte count for a patient with bronchial asthma with afebrile pertussis treated with intramuscular injections of venom protein (crotalin) solution. The letters have the following meaning: *A*, it was learned that two sisters of the patient have pertussis; *B*, onset of mild coughing spells; *C*, onset of moderate coughing spasms; *D*, onset of severe spells of coughing spasms; *E*, moderate coughing spells; *F*, mild coughing spells; *G*, cessation of cough. In this chart and in the other charts the solid line indicates eosinophils; the dash line, polymorphonuclears, and the dotted line, lymphocytes. Blood counts recorded on the days of injection were performed prior to injection. The monocytes and basophils are not recorded because they did not appear to be of any significance. *X* indicates an attack of asthma or spell of wheezing. The local reaction occurring at the site of the injection of crotalin solution is recorded as follows: neg indicates negative; sl, slight; v. sl, very slight; m, moderate, and s, severe or intense.

sisters were ill with pertussis. After April 19 the patient had a slight cough but remained free from asthma. There was no definite change in the percentage of eosinophils until May 5, when the count dropped to 4 per cent; the proportion of lymphocytes rose to 71 per cent, and, the number of polymorphonuclears fell to 25 per cent. The diagnosis of pertussis was established. For the following two weeks during the height of pertussis the lymphocyte count ranged between 70 and 80 per cent, while with the exception of two instances (May 6 and 13) the

eosinophil count remained at normal levels. The slight rise of the proportion of eosinophils to 7 and 6 per cent, respectively, in the two instances mentioned occurred one day after the injection of venom solution. On May 26 the cough was mild (the eosinophils numbered 7 per cent; the lymphocytes, 48 per cent, and the polymorphonuclears, 49 per cent), and on June 10 it had stopped (the eosinophil count was 22 per cent; the lymphocyte count, 40 per cent, and the polymorphonuclear count, 35 per cent). Thereafter the incidence of lymphocytes remained around normal levels which, however, were generally higher than the percentage of lymphocytes encountered prior to the incubation period of pertussis. The polymorphonuclears showed a relative decrease.

On July 20, the patient was sent to the country, where he contracted measles. He returned home about September 6 and continued to remain free from asthma until October 13, when wheezing set in. The asthmatic symptoms became progressively worse, and in December the attacks were severe and frequent.

The freedom from asthma in this patient over a period of six months was attributed more to the influence of the afebrile pertussis and measles than to that of the nonspecific crotalin therapy. However, it is of extreme clinical interest to note that during the severe paroxysmal stage of pertussis and despite the

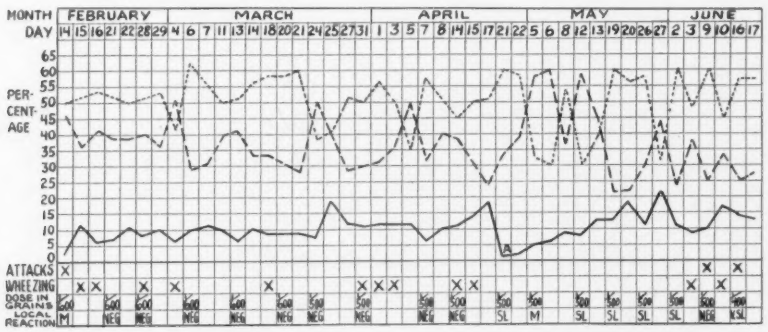

Chart 2 (case 2).—Differential leukocyte count for patient with bronchial asthma with intercurrent grip treated with intramuscular injections of venom protein (crotalin) solution. *A* indicates that on May 21 the patient had grip with a temperature of 102 F., and was confined to bed for the following ten days with an elevation of temperature of varying degrees.

continuation of the injections of crotalin, the eosinophilic index was depressed to within normal limits. It was not until the final stage of pertussis that eosinophilia reappeared under the influence of crotalin. In this case it seemed that the depressing influence of the pertussis infection on the eosinophil cells overwhelmed the stimulating influence of the crotalin venom solution.

CASE 2.—V. V., a boy, was 2 years of age at the onset of asthma. He first came under observation in 1922, at the age of 4 years, when allergy studies showed him to be sensitive to various animal inhalant substances, orris root and house dust. The asthmatic attacks were severe and occurred frequently. In 1928, eighteen injections of venom protein solution were given, and forty-five differential leukocyte counts were made over a period of one hundred and twenty-three days (chart 2). The maximum dose of crotalin was maintained at 0.14 mg. (1/500 grain) because this child showed on previous occasions tolerance for only small doses of specific and nonspecific antigens. Prior to the initial injection of 0.1 mg. of crotalin the eosinophilic index was 3 per cent, and on the following day it rose

to 12 per cent. For the following five weeks the dose of crotalin remained the same, and the eosinophilic index ranged between 6 and 11 per cent. On March 24, the eosinophil count was 8 per cent, and 0.14 mg. of crotalin was injected. The next day the eosinophils rose to 19 per cent. With the subsequent doses of crotalin unchanged the eosinophilic index mounted to higher levels than when the doses were 0.1 mg., with the exception of the two weeks period beginning May 21. On the latter day the child had a grippal infection, with a temperature of 102 F., and the eosinophil count was 1 per cent. The temperature remained elevated for ten days.

The asthma in this case was definitely improved for a period of two months as a result of crotalin therapy and continued to remain so for another month following the grippal infection. However, attacks of asthma returned in their usual severe form and continued for several months thereafter. Of extreme interest in this case is the observation that while the patient had a grippal infection with an elevation of temperature eosinopenia occurred and the injection of crotalin solution failed to cause a rise of the eosinophil count above the normal level.

CASE 3.—I. R., a boy, was 2 years old at the onset of asthma. He was first seen in 1926, at the age of 7 years, when the skin tests showed positive reactions

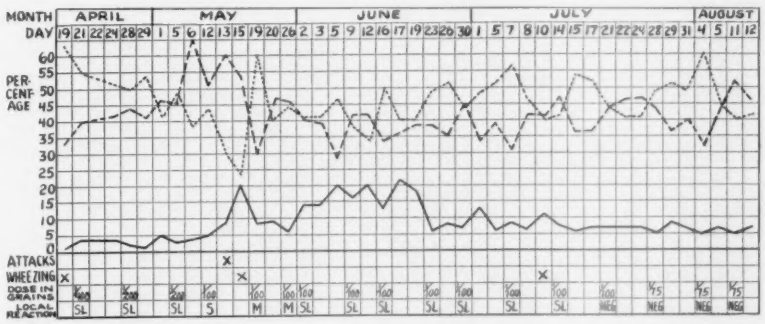

Chart 3 (case 3).—Differential leukocyte count for a patient with bronchial asthma treated with intramuscular injections of venom protein (crotalin) solution.

to the biologic fish groups, animal inhalants, cottonseed and house dust. Attacks of asthma occurred perennially at intervals of about every two weeks. In 1928, seventeen injections of venom protein solution were given over a period of one hundred and fifteen days, the maximum dose being 0.85 mg. (1/75 grain), and the differential leukocyte counts totaled 44 (chart 3). The eosinophil counts prior to the initial injection of 0.18 mg. (1/400 grain) of crotalin were normal and remained so until 0.65 mg. (1/100 grain) was injected on May 12. On the following day an attack of asthma set in, and on the third day after the injection the eosinophil count rose to 20 per cent. Under the influence of crotalin therapy the eosinophilic index maintained high levels until July 15, when it fell to 6 per cent; it remained around this level in spite of the fact that the dose of crotalin was increased to 0.85 mg. (1/75 grain). Treatment was discontinued on August 11. The patient continued to remain free from attacks of asthma until August 1930, when he contracted a ragweed pollen allergy.

The relief from asthma for a period of two years in this case can be attributed to the nonspecific protection afforded by crotalin therapy. The so-called "nonspecific desensitization" is clearly demonstrated if one accepts the eosinophilic index as a means of determining allergic hyposensitization.

Case 4.—E. G., a boy, was 7½ years old at the onset of asthma. He first came under observation in 1926, at the age of 9 years, when protein skin tests showed positive reactions to many food and inhalant substances, including ragweed pollen; there was no history of pollen allergy. The attacks of asthma were severe and frequent. They occurred perennially and were more pronounced during the winter months. In 1928, during one hundred and one days, fifteen injections of venom protein solution (maximum dose, 0.18 mg.) were administered, and thirty-two differential leukocyte counts were made (chart 4). Prior to the initial injection of 0.14 mg. of crotalin the eosinophilic index was 10 per cent. On June 20, the eosinophilic index rose to 31 per cent. Thereafter, with a stationary dose of 0.18 mg. of crotalin the eosinophil curve showed a definite tendency to become progressively lower, and prior to the last injection of crotalin, on August 16, the eosinophil count dropped to 8 per cent.

Under the influence of small doses of crotalin over a period of three months this patient showed definite clinical improvement, remaining free from all attacks of asthma from June 27 to October 28. That winter mild attacks occurred at frequent intervals. Crotalin therapy was continued to February 1930, and the

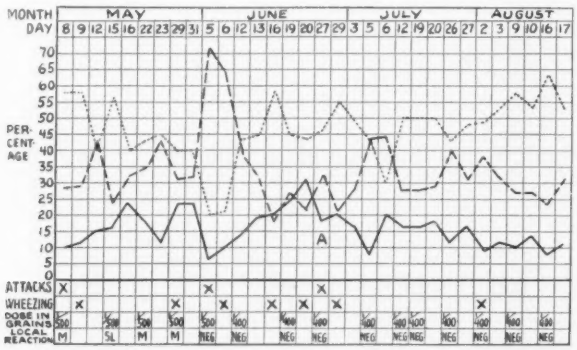

Chart 4 (case 4).—Differential leukocyte count for a patient with asthma treated with intramuscular injections of venom protein (crotalin) solution. *A* indicates that from June 24 to 27, inclusive, the patient had severe attacks of asthma initiated by an afebrile infection of the upper respiratory tract.

patient showed progressive improvement. In September symptoms of ragweed pollen allergy made its first appearance, and specific treatment was instituted.

Case 5.—G. M., a boy, was 3½ years old at the onset of asthma. He was first observed in 1926, at 6 years of age, when skin tests showed positive reactions to many foods; horse, rabbit and dog danders; ragweed, and house dust. Attacks of asthma occurred perennially at intervals of from two to three weeks, with no clinical evidences of pollen allergy. In 1926, following the institution of dietetic measures and avoidance of exposure to the inhalants to which he was sensitive, the patient was markedly relieved from asthma. Asthma recurred during the winter of 1927.

In 1928, eighteen injections of crotalin (maximum dose, 0.65 mg.) were administered over a period of two hundred and twelve days, during which time fifty-three differential leukocyte counts were made (chart 5). Prior to the initial injection of 0.1 mg. of crotalin the eosinophil counts were 6 and 8 per cent, respectively. Under the influence of crotalin therapy the eosinophilic index rose to as high as 24 per cent.

The patient was sent to the country for one month, beginning August 18. There he remained entirely well, except for two brief mild attacks of asthma following the eating of cherries. He remained free from asthma until June 1929, when he had a few attacks. He was again sent to the country for three and one-half months, where he was entirely well and remained so until July 29, 1931, when he was last seen.

The improvement in this case can be more reasonably attributed to the changes of environment over a period of two summers than to crotalin therapy, which, however, may have had a contributing beneficial influence. During the course of crotalin therapy it appeared that when the eosinophil count remained above rather than below 8 per cent the patient remained free from attacks of asthma.

Case 6.—A. K., a boy, was 15 months old at the onset of asthma. He was first observed in 1922, at the age of 2 years, when he had enlarged bronchial (nontuberculous) glands which caused partial bronchostenosis with typical asthmatic symptoms (para-asthma).[5] Roentgen therapy resulted in complete relief from all symptoms. The protein skin reactions were negative, and eosinophil counts were

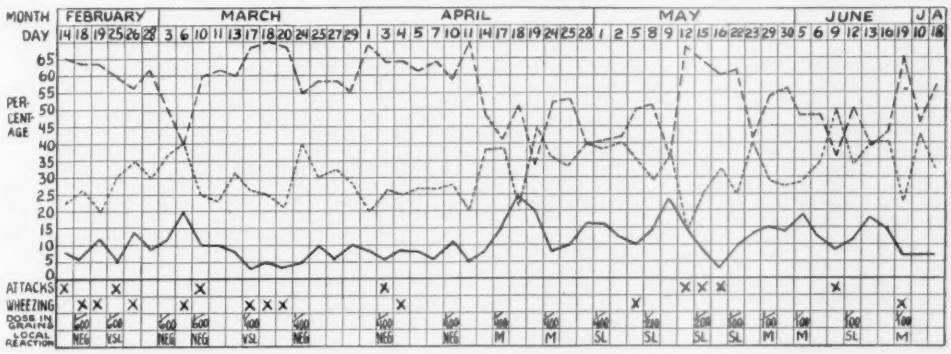

Chart 5 (case 5).—Differential leukocyte count for a patient with bronchial asthma treated with intramuscular injections of venom protein (crotalin) solution. *J* indicates July, and *A*, August.

1 per cent. In 1925, following a series of recurrent infections of the upper respiratory tract, asthma recurred; the skin reactions were again negative. Nonspecific therapy (stock bacterial vaccine and milk) in repeated courses relieved the patient of all asthmatic symptoms for varying periods.

On April 19, 1928, the child had been free from asthma for one month, so injections of venom protein solution were begun to determine its influence on the eosinophil count under these conditions. Eighteen injections were given (maximum dose, 0.65 mg.) over a period of one hundred and twenty-two days, and thirty-seven differential leukocyte counts were made (chart 6). Prior to the initial dose of 0.35 mg. (1/200 grain) of crotalin the eosinophil counts were 6 and 8 per cent, respectively. With the dose of crotalin kept the same for the first fifteen injections and the patient entirely free from asthma the eosinophil count rose to as high as 28 per cent, but the rise did not begin until after the fourth

5. Peshkin, M. M.: Asthma in Children: I. Etiology, Am. J. Dis. Child. **31**:763 (June) 1926. Peshkin, M. M., and Fineman, A. H.: Acute Massive Atelectasis and Asthma, ibid. **42**:590 (Sept.) 1931.

injection. On July 28 (fifteenth injection), the eosinophil count dropped to 6 per cent, thus suggesting a tendency to lack of eosinophilic response to a stationary dose of crotalin. In spite of this phenomenon, the patient coughed for one week, beginning July 28, and had a wheezing spell on August 4.

After a stay of four weeks in the country, where the patient remained free from all symptoms of asthma, he returned to his home on September 20. Two weeks later he contracted acute rhinitis, which was followed by severe asthma lasting four days.

The nonspecific protection of crotalin therapy in this case was nil. The patient remained well during the period when the eosinophil count was at higher levels.

Case 7.—A. Y., a boy, was 8 years old at the onset of asthma. In 1925, when he was 14 years of age, the protein skin tests showed positive reactions to egg, chicken meat, beef, lamb and feather epithelium. The patient had arrested pul-

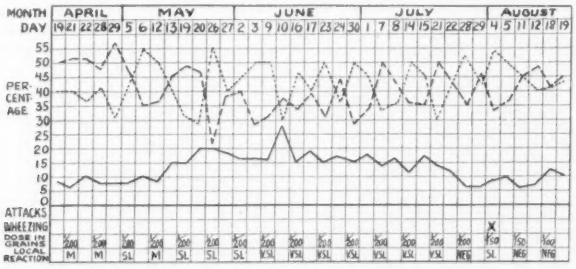

Chart 6 (case 6).—Differential leukocyte count for a patient with asthma treated with intramuscular injections of venom protein (crotalin) solution.

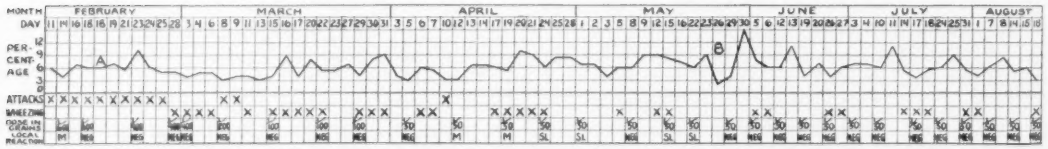

Chart 7 (case 7).—Eosinophil count for a patient with bronchial asthma treated with intramuscular injections of venom protein (crotalin) solution. *A* indicates that a differential blood count was done one hour after injection; *B* indicates the onset of a grippal infection, with elevation of temperature for the following two days.

monary tuberculosis. Asthma was usually associated with infections of the upper respiratory tract and was especially severe during the three months preceding February 1928, at which time crotalin therapy was begun.

Thirty injections of venom protein solution (maximum dose of crotalin, 1.2 mg.) were given over a period of one hundred and eighty-five days, and eighty-one differential leukocyte counts were made (chart 7). Prior to the initial injection of crotalin on February 14, the eosinophil counts were 4 and 6 per cent, respectively. Severe asthmatic symptoms continued to March 9, with no definite increase in the number of eosinophils except for one occasion, when the count rose to 10 per cent. Thereafter to August 18, when crotalin therapy was discontinued, the patient had only one attack of asthma but many wheezing spells. As the wheezing spells were becoming less frequent, progressively milder and of shorter duration the eosinophilic index showed a tendency to maintain a level above 7 per cent. On

May 26, the patient had a grippal infection, with an elevation of temperature, and the eosinophil count dropped from 9 to 2 per cent. The following winter asthma recurred with its former frequency and severity.

The temporary apparent improvement from asthmatic symptoms in this case can be attributed to the influence of the season of the year (summer) rather than to the influence of crotalin therapy. However, during this state the eosinophil counts showed a tendency to maintain higher levels than when asthma was severe. Of interest in this case is the fact that despite the continuation of crotalin therapy the eosinophils dropped to 2 per cent in the presence of a grippal infection.

CASE 8.—M. H., a girl, was 4½ years old at the onset of asthma. She was first observed in 1925, when she was 11 years of age. Protein skin tests showed positive reactions to goose, pork, horse dander and horse serum. Asthma was perennial and appeared in an aggravated form for the two months prior to the institution of crotalin therapy in February 1928.

Twenty-three injections of crotalin (maximum dose, 1.2 mg.) were administered over a period of one hundred and sixty-one days, during which time fifty-seven differential leukocyte counts were made (chart 8).

Prior to the initial injection of 0.1 mg. of crotalin on February 11, the eosinophil count was 2 per cent. Thereafter until April 21, after eleven injections of increasing doses of crotalin, the eosinophil counts remained within normal limits, and the asthmatic attacks were mild, less frequent and of shorter duration.

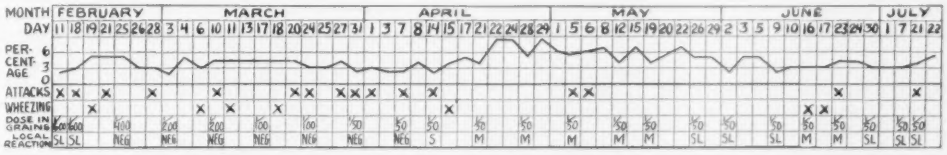

Chart 8 (case 8).—Eosinophil count for a patient with bronchial asthma treated with intramuscular injections of venom protein (crotalin) solution.

For the month following April 22 the eosinophil counts showed a tendency to remain above normal levels and at times rose to 8 per cent. During the latter period the patient had asthma for only two days. During the subsequent and last two months of treatment the eosinophil counts again were within normal limits, but the patient was having asthmatic symptoms.

In the fall of 1928 and the following winter months, asthma recurred with its former frequency and intensity. In 1929, the patient was sent to the country for a period of five months, where she showed marked improvement, and since 1930 she has remained entirely free from asthma.

Under the influence of increasing doses of crotalin this patient did not begin to have eosinophilia until after the eleventh injection. The period of eosinophilia did not last more than one month, during which time she appeared more free from asthmatic symptoms than at any other time during the five month course of treatment.

CASE 9.—M. F., a boy, was 6 years old at the onset of asthma. He was first observed in 1927, at the age of 13 years, when the cutaneous tests showed positive reactions to horse, dog and chicken epithelium and house dust. Attacks of asthma occurred frequently and were of the perennial type, with some remission during the summer months.

In 1928, seventeen injections of crotalin (maximum dose, 1.2 mg.) were administered over a period of one hundred and sixteen days, during which time thirty-two differential leukocyte counts were made (chart 9).

Prior to the initial injection of 0.18 mg. of crotalin on April 21, the eosinophil count was 6 per cent. Under the influence of crotalin therapy the eosinophil count rose to 12 per cent. During the last seven weeks of treatment the eosinophil count remained within normal limits. For one month, beginning August 16, the child was in the country, where he had two attacks of asthma. On his return home asthma recurred in its usual form.

The normal eosinophil counts occurring during the last eight injections of crotalin suggest a lack of eosinophilic response to crotalin. The temporary improvement occurring during the summer months is credited to the season of the year rather than to the effect of crotalin therapy.

Case 10.—S. D., a boy, was 9½ years old at the onset of asthma. In 1926, at the age of 10 years, when he was first observed, the cutaneous tests showed positive reactions to brazil-nut, tomato, dog hair and house dust. The patient was

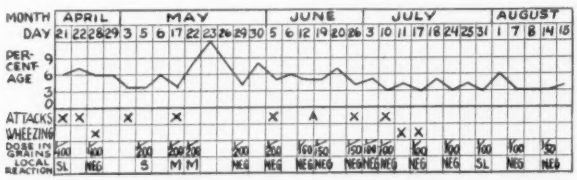

Chart 9 (case 9).—Eosinophil count for a patient with bronchial asthma treated with intramuscular injections of venom protein (crotalin) solution. *A* indicates that an attack of asthma occurred on June 14.

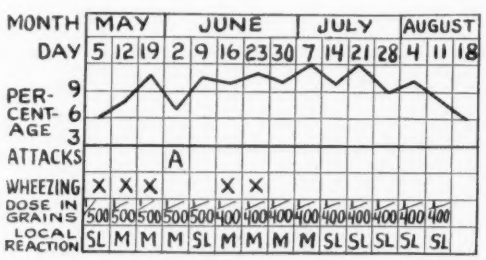

Chart 10 (case 10).—Eosinophil count for a patient with bronchial asthma treated with intramuscular injections of venom protein (crotalin) solution. *A* indicates that an attack of asthma occurred on May 26.

markedly relieved from asthma until the end of April 1928, when he began to cough, and soon continual wheezing spells set in.

The differential leukocyte counts in this case could be performed only prior to the injections of crotalin solution. Fourteen injections were administered over a period of one hundred and five days. During this time fifteen differential leukocyte counts were made (chart 10).

Prior to the initial injection of 0.14 mg. of crotalin the eosinophilic index was 6 per cent. During the course of treatment over a period of three and one-half months the eosinophilic index ranged mostly between 9 and 12 per cent. Beginning with the last two months of treatment, the patient remained free from asthma and continued so until May 11, 1929, when asthma recurred intermittently for the following two and one-half months. A second course of injections of crotalin given at weekly intervals was administered from January to October 1929. Asthma recurred again in September over a period of one month. In May 1930, skin

tests showed positive reactions to ragweed and grass pollens, thus confirming the diagnosis of pollen asthma in the summer and fall made in the summer of 1929.

The second course of crotalin therapy extended over a period of nine months, which included the pollen seasons, and did not alter the course of pollen asthma in 1929. The influence of venom protein solution given in 1928 again demonstrated its power to maintain an increase in the eosinophilic index, during which time the patient was free from all asthmatic symptoms.

CASE 11.—F. A., a boy, was 6 years old at the onset of asthma. In 1927, when the patient was 10 years of age, the skin tests showed positive reactions to horse, cat, dog and rabbit epithelium. Attacks of asthma occurred almost monthly, and frequent wheezing spells occurred between attacks.

In 1928, twenty-five injections of venom protein solution were administered over a period of one hundred and seventy-eight days, and fifty-six differential leukocyte counts were made (chart 11).

Prior to the initial injection of 0.1 mg. of crotalin on February 18, the eosinophil count was 4 per cent. During the following six months the number of eosinophil cells rose to 12 per cent, with the tendency to remain above the normal level. Marked relief from asthmatic symptoms set in after the seventh injection of crotalin on April 5. The last differential count was made on August 15. However, the injections of crotalin were continued at weekly and later at biweekly

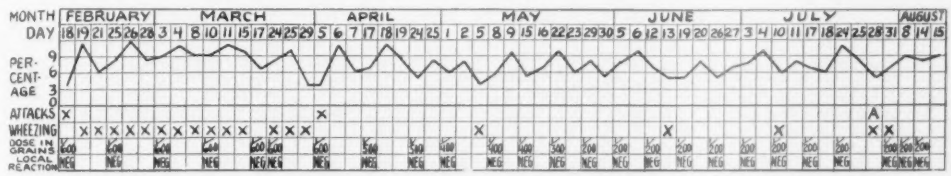

Chart 11 (case 11).—Eosinophil count for a patient with bronchial asthma treated with intramuscular injections of venom protein (crotalin) solution. *A* indicates that an attack of asthma occurred on July 26.

intervals to November 1932, when a total of one hundred and two injections of venom protein solution were administered. During the last three years of treatment with crotalin the patient seldom wheezed or had an attack of asthma.

The beneficial influence of crotalin therapy in this case was maintained over a period of four years, and during the first six months of treatment when differential leukocyte counts were made the eosinophil cells showed a tendency to remain above normal levels.

MILK

Sterilized milk (whole or skimmed) with a high bacterial count is commonly employed as a nonspecific antigen for injection in the treatment of bronchial asthma.

Thirteen children with bronchial asthma (seven with positive and six with negative reactions) were given injections of sterilized skimmed milk of a high bacterial content. The number of injections of milk per patient and the maximum dose employed without inducing a "fever reaction" in these children permit observation from which definite conclusions with regard to the influence of milk on the eosinophilic index can be drawn. The findings are set forth in table 1.

TABLE 1.—*Differential Leukocyte Count for Thirteen Children with Bronchial Asthma Given Injections of Milk with a High Bacterial Count*

	Date	Number of Injections	Dose in Cc.	Differential Leukocyte Count, Percentage*			Comment
				Polymorphonuclear Neutrophils	Lymphocytes	Eosinophils	
Patient 12, S. G., a girl, aged 7 years; age of onset of asthma, 2 years†	10/30/30	1	0.5	31	62	2	Attacks of asthma and wheezing spells
	11/ 6	2	1.0	..	..	..	Wheezing
	11/ 8	3	1.5	32	63	1	Wheezing
	11/13	4	2.0	..	..	..	Wheezing
	11/18	5	2.5	..	..	..	Well
	11/20	6	3.0	34	60	3	Well
	11/25	7	3.0	..	..	..	Well
	12/ 2	8	3.0	..	..	..	Wheezing
	12/12	9	3.0	29	63	3	Well
	12/26	10	3.0	..	..	..	Wheezing
	1/ 6/31	11	3.0	..	..	..	
	1/13	12	3.0	..	..	..	
	1/20	13	3.0	32	62	2	Much wheezing
	1/27	14	3.0	31	63	3	Much wheezing
Patient 13, M. S., a girl, aged 2½ years; age of onset of asthma, 1½ years	5/16/31	1	0.5	45	42	9	Wheezing and coughing
	5/19	2	1.0	..	..	..	
	5/23	3	1.5	42	43	10	Slight wheezing
	5/26	4	2.0	..	..	..	Slight wheezing
	5/28	5	2.5	..	..	..	Slight wheezing
	6/ 1	6	3.0	46	41	10	Wheezing and coughing
	6/ 8	7	3.0	..	..	..	
	6/15	8	3.0	45	42	11	Wheezing and coughing
	6/22	9	3.0	..	..	..	Wheezing and coughing
	6/29	10	3.0	..	..	..	Wheezing and coughing
	7/ 2	11	3.0	48	40	8	Wheezing and coughing
	7/ 3	..	....	43	44	8	Wheezing and coughing
Patient 14, M. G., a boy, aged 15 years; age of onset of asthma, 6 years	7/31/28	1	0.5	42	53	3	Attacks of asthma and wheezing
	8/ 2	2	1.0	63	28	4	Wheezing
	8/ 4	3	1.0	44	50	3	Mild attack
	8/ 7	4	1.0	52	37	8	Well
	8/ 8	..	....	60	30	6	Well
	8/ 9	5	1.5	48	43	6	Well
	8/10	6	2.0	57	35	5	Slight wheezing
	8/11	..	....	47	44	6	Slight wheezing
	8/12	..	....	50	40	8	Slight wheezing
	8/14	7	2.5	60	30	5	Moderate wheezing
	8/15	..	....	55	36	6	Well
	8/16	8	3.0	50	41	6	Well
	8/18	9	3.0	55	34	8	Well
	8/19	..	....	49	32	6	Well
Patient 15, B. B., a girl, aged 11 years; age of onset of asthma, 5½ years†	10/23/34	..	....	45	48	6	Much coughing only
	10/26	..	....	35	60	1	Cough only on 10/24
	10/30	1	0.5	49	45	1	Occasional cough
	11/ 1	2	1.0	59	36	3	Well
				41	53	4‡	
	11/ 3	3	1.5	43	49	4	Well
				45	48	3‡	
	11/ 6	4	2.0	40	52	4	Well
				39	55	4‡	
	11/ 8	5	2.5	54	41	2	Well
				57	39	2‡	
	11/10	6	3.0	51	45	2	Well
				49	45	3‡	
	11/13	7	3.0	46	49	1	Well
				42	48	3‡	
	11/15	..	....	56	40	1	Well
	11/17	8	3.0	42	53	3	Well
				34	61	2‡	
	11/20	9	3.0	42	53	2	Well
				37	58	2‡	
	11/22	..	....	48	45	3	Well
	11/24	10	3.0	47	47	4	Well
				48	46	3‡	
	11/27	11	3.0	41	54	3	Well
				42	54	2‡	

* The basophils and monocytes were omitted for the reason stated in the legend of chart 1.
† A nonreactor by the cutaneous test.
‡ A differential leukocyte count was performed one hour after injection of crotalin solution.

TABLE 1.—*Differential Leukocyte Count for Thirteen Children with Bronchial Asthma Given Injections of Milk with a High Bacterial Count—Continued*

	Date	Number of Injections	Dose in Cc.	Differential Leukocyte Count, Percentage*			Comment
				Polymorphonuclear Neutrophils	Lymphocytes	Eosinophils	
Patient 15, continued	12/ 1	12	3.0	34	62	2	Well
				38	56	5‡	
	12/ 4	13	3.0	43	53	3	Well
				40	53	4‡	
	12/ 6	..	...	51	44	2	Well
	12/ 8	..	...	44	46	4	Well
	12/11	..	...	48	46	4	Mild acute rhinitis since 12/9
	12/15	..	...	43	53	2	Well
	12/18	..	...	46	49	2	Well
	12/22	..	...	69	25	1	Well
Patient 16, E. F., a boy, aged 5 years; age of onset of asthma, 2¼ years	10/23/34	..	...	57	29	11	Occasional wheezing at night
	10/25	..	...	50	38	10	Occasional wheezing at night
	11/ 1	1	0.5	51	38	9	Intermittent wheezing
	11/ 3	2	1.0	52	41	6	Cough only
	11/ 6	3	1.5	54	32	10	Slight wheezing at night
	11/ 8	4	2.0	53	36	8	Well
	11/10	5	2.5	55	34	9	Well
	11/13	6	3.0	50	37	11	Well
	11/15	7	3.0	46	40	9	Well
	11/17	8	3.0	50	33	6	Well
	11/20	9	3.0	50	38	6	Slight wheezing on 11/19
	11/22	..	...	41	45	12	Well
	11/24	10	3.0	46	39	9	Well
	11/27	11	3.0	46	38	12	Well
	12/ 1	12	3.0	59	26	12	Severe pertussoid cough immediately after injection
	12/ 4	13	3.0	46	40	10	Well
	12/ 6	..	...	56	30	10	Wheezing for one hour on 12/5
	12/11	..	...	45	42	9	Attack of asthma for three days beginning 12/7
	12/15	..	...	42	34	21	Slight wheezing at night only
	12/18	..	...	52	33	11	Attack of asthma on 12/16; slight wheezing since
Patient 17, J. M., a boy, aged 6 years; age of onset of asthma, 3 years	10/23/34	..	...	32	58	6	Slight wheezing
	10/25	..	...	24	58	12	Slight wheezing
	10/27	..	...	53	38	5	Slight wheezing
	10/30	1	0.5	44	41	11	Slight cough only
	11/ 2	2	1.0	26	54	15	Slight cough only
				28	53	13‡	
	11/ 3	3	1.5	39	45	11	Watery nasal discharge and slight cough
				43	44	10‡	
	11/ 8	4	1.5	51	33	13	Attack of asthma for three days from 11/4
				46	36	16‡	
	11/10	5	2.0	52	35	10	Well
				49	35	12‡	
	11/13	6	2.5	32	45	21	Well
				29	58	14‡	
	11/15	7	3.0	34	52	11	Well
				33	47	15‡	
	11/17	8	3.0	39	46	13	Occasional cough for past two days
				37	49	11‡	
	11/20	9	3.0	32	52	13	Very slight cough daily
				28	60	9‡	
	11/22	..	...	37	53	8	Slight wheezing
	11/24	10	3.0	47	41	10	Slight wheezing 11/23
				45	43	6‡	
	11/27	11	3.0	30	53	15	Well
				29	53	13‡	
	12/ 1	12	3.0	25	58	14	Wheezing on 11/9 and 11/30
				25	59	13‡	
	12/ 4	13	3.0	47	40	8	Wheezing only
				37	52	8‡	
	12/ 6	..	...	34	46	17	Slight cough only
	12/ 8	14	3.0	35	51	11	Well
				34	54	9‡	
	12/11	..	...	35	45	15	Well
	12/18	..	...	34	46	15	Well
	12/22	..	...	62	25	7	Well

* The basophils and monocytes were omitted for the reason stated in the legend of chart 1.
† A nonreactor by the cutaneous test.
‡ A differential leukocyte count was performed one hour after injection of crotalin solution.

TABLE 1.—*Differential Leukocyte Count for Thirteen Children with Bronchial Asthma Given Injections of Milk with a High Bacterial Count—Continued*

	Date	Number of Injections	Dose in Cc.	Differential Leukocyte Count, Percentage*			Comment
				Polymorphonuclear Neutrophils	Lymphocytes	Eosinophils	
Patient 18,	10/28/34	..	...	39	47	9	Coughing
A. P., a girl,	10/30	1	0.5	39	48	10	Coughing
aged 5 years;	11/ 1	2	1.0	46	47	6	Coughing and nasal discharge
age of onset	11/ 3	3	0.5	41	50	8	Slight wheezing and discharge
of asthma,	11/ 8	4	1.5	34	55	6	Wheezing
6 months	11/15	5	1.5	35	56	5	Attack of asthma on 11/14
	11/17	6	2.0	51	40	7	Wheezing
	11/20	7	2.5	44	48	5	Well
	11/22	8	3.0	40	46	11	Slight coughing only
	11/27	9	3.0	35	53	10	Slight wheezing occasionally
	12/ 1	10	3.0	38	45	14	Coughing only
	12/ 4	11	3.0	38	49	11	Sneezing last two days and wheezing this morning; one-half minute after injection patient coughed spasmodically and acute asthma set in; subcutaneous injection of 5 minims of epinephrine hydrochloride (1:1,000) controlled all symptoms; anaphylactoid shock
	12/11	12	3.0	31	47	19	Slight wheezing; elevation of temperature up to 102 F. on 12/4; intradermal reaction to milk negative
	12/15	13	3.0	47	33	19	Slight cough only
	12/18	..	...	27	53	17	Only slight cough and wheezing during nights
	12/29	..	...	43	45	10	Confined to bed during past week with acute rhinitis and tonsillitis; no asthma
Patient 19,	3/25/33	..	...	51	44	3	Well
C. L., a girl,	6/29	..	...	34	61	2	Wheezing
aged 9½ years;	8/10	..	...	38	58	2	Well
age of onset	10/24	..	...	34	62	3	Well
of asthma,	1/27/34	..	...	45	52	2	Slight wheezing
2 years	4/14	..	...	36	58	3	Well
	6/21	..	...	40	57	2	Wheezing this morning
	9/ 4	..	...	29	67	2	Occasional cough
	10/23	..	...	40	55	4	Coughing last two days
	10/25	..	...	34	59	5	Well
	10/27	..	...	34	58	5	Well
	10/30	1	0.5	35	53	7	Slight cough in morning
	11/ 1	2	0.5	36	55	5	Well
	11/ 3	3	0.5	37	55	5	Well
	11/ 6	4	1.0	35	56	6	Well
	11/ 8	5	1.5	45	46	6	Well
	11/10	6	2.0	41	53	4	Well
	11/13	7	2.5	61	30	6	Well
	11/15	8	3.0	40	55	3	Well
	11/17	9	3.0	35	55	5	Well
	11/20	10	3.0	37	52	5	Very mild cough
	11/22	..	...	45	48	5	Very mild cough
	11/24	11	3.0	40	51	7	Well
	11/27	12	3.0	49	44	5	Well
	12/ 1	13	3.0	41	56	1	Well
	12/ 4	14	3.0	38	54	5	Mild cough this morning
	12/ 6	..	...	38	58	2	Mild cough this morning
	12/ 8	15	3.0	50	44	2	Well
	12/11	16	3.0	40	54	5	Coughing in the morning
	12/18	..	...	33	57	6	Attack of asthma on 12/15
Patient 20,	2/16/33	..	...	51	41	5	Well
F. S., a girl,	6/ 3	..	...	45	41	8	Slight wheezing
aged 9 years;	2/17/34	..	...	55	40	2	Slight wheezing for last 4 days
age of onset	8/21	..	...	48	49	1	Well
of asthma,	10/23	..	...	49	46	2	Cough only for the last week
5 years†	10/25	..	...	50	43	3	Less coughing
	10/27	..	...	45	49	3	Only slight cough

* The basophils and monocytes were omitted for the reason stated in the legend of chart 1.
† A nonreactor by the cutaneous test.

TABLE 1.—*Differential Leukocyte Count for Thirteen Children with Bronchial Asthma Given Injections of Milk with a High Bacterial Count—Continued*

	Date	Number of Injections	Dose in Cc.	Differential Leukocyte Count, Percentage*			Comment
				Polymorphonuclear Neutrophils	Lymphocytes	Eosinophils	
Patient 20, continued	10/30	1	0.5	48	46	2	Well
				50	44	2	One hour after injection
	11/ 1	2	1.0	51	42	2	Well
	11/ 3	3	1.5	40	51	6	Well
	11/ 6	4	2.0	53	39	4	Well
	11/ 8	5	2.5	46	48	2	Well
	11/10	6	3.0	39	55	2	Well
	11/13	7	3.0	46	49	2	Well
	11/15	..	...	47	48	1	Well
	11/17	8	3.0	45	49	2	Well
	11/20	9	3.0	53	41	2	Well
	11/22	..	...	58	34	4	Well
	11/24	10	3.0	37	52	5	Well
	11/27	11	3.0	37	58	3	Well
	12/ 1	12	3.0	36	57	5	Well
	12/ 4	13	3.0	46	46	4	Well
	12/11	..	...	45	48	3	Well
	12/15	..	...	48	46	2	Well
	12/18	..	...	52	42	2	Well
Patient 21, J. S., a boy, aged 12 years; age of onset of asthma, 6½ years†	2/25/33	..	...	42	41	13	Coughing
	6/24	..	...	48	40	6	Wheezing last night
	9/16	..	...	57	29	9	Well all summer; wheezing for past week
	11/25	..	...	48	38	11	Wheezing badly every night
	2/ 3/34	..	...	34	54	11	Well
	7/26	..	...	40	52	6	Well
	9/22	..	...	44	41	12	Wheezing slightly this morning
	10/23	..	...	44	45	8	Frequent respiratory oppression
	10/25	..	...	53	36	6	Slight coughing
	10/27	..	...	41	43	12	Well
	10/30	1	0.5	54	28	16	Well
	11/ 1	2	1.0	44	38	15	Only slight coughing
				55	28	13‡	
	11/ 3	3	1.5	45	42	10	Less coughing; occasional wheezing
				57	26	13‡	
	11/ 6	4	2.0	46	35	15	Well
				42	38	16‡	
	11/ 8	5	2.5	51	35	11	Well
				45	38	12‡	
	11/10	6	3.0	43	37	15	Well
				48	38	8‡	
	11/13	7	3.0	44	40	13	Wheezing yesterday
				55	26	14‡	
	11/15	..	...	53	36	1	Well; differential count checked
	11/17	8	3.0	48	40	5	Well
				39	45	7‡	
	11/20	9	3.0	47	42	8	Well
				47	43	8‡	
	11/22	..	...	46	41	8	Well
	11/24	10	3.0	47	41	7	Well
				49	40	7‡	
	11/27	11	3.0	44	41	11	Well
				45	38	12‡	
	12/ 1	12	3.0	44	42	10	Well
				39	47	11‡	
	12/ 4	13	3.0	39	42	13	Well
				40	48	10‡	
	12/ 6	..	...	47	34	16	Well
	12/ 8	14	3.0	43	40	13	Well
				50	33	13	
	12/11	..	...	54	31	13	Only slight cough since 12/8
	12/15	..	...	41	42	12	Condition unchanged
	12/18	..	...	61	28	6	Well since 12/16
	12/22	..	...	75	15	3	Much coughing at night since 12/19
Patient 22, A. L., a girl, aged 11¾ years; age of onset of asthma, 10 years†	5/13/33	..	...	39	44	12	Well
	6/22	..	...	48	39	9	Sneezing and wheezing at night
	8/10	..	...	51	36	9	Well
	9/14	..	...	44	43	11	Wheezing
	11/ 9	..	...	52	31	12	Sneezing and coughing on 11/8

* The basophils and monocytes were omitted for the reason stated in the legend of chart 1.
† A nonreactor by the cutaneous test.
‡ A differential leukocyte count was performed one hour after injection of crotalin solution.

TABLE 1.—*Differential Leukocyte Count for Thirteen Children with Bronchial Asthma Given Injections of Milk with a High Bacterial Count—Continued*

	Date	Number of Injections	Dose in Cc.	Differential Leukocyte Count, Percentage*			Comment
				Polymorphonuclear Neutrophils	Lymphocytes	Eosinophils	
Patient 22, continued	7/24/34	..	...	52	35	10	No asthma for past 9 months
	9/13	..	...	50	36	12	Respiratory oppression for last 3 days
	10/25	..	...	44	43	12	Less respiratory oppression
	10/30	1	0.5	40	46	9	Well
				41	43	12	
	11/ 1	2	1.0	35	45	18	Well
	11/ 3	3	1.5	40	48	8	Well
				44	51	4	
	11/ 6	4	2.0	43	37	17	Well
				38	42	19‡	
	11/ 8	5	2.5	35	42	20	Well
				46	43	8‡	Differential count checked
	11/10	6	3.0	50	36	12	Well
				43	41	13‡	
	11/13	7	3.0	36	50	12	Well
				40	46	12‡	
	11/15	..	...	39	48	9	Well
	11/17	8	3.0	41	47	9	Well
				39	43	13‡	
	11/20	9	3.0	48	39	6	Acute rhinitis on previous day
				42	40	8‡	
	11/22	..	...	27	53	16	Nasal condition unchanged; slight wheezing; temperature 100 F.
	11/24	10	3.0	30	55	14	Well
				30	53	14‡	
	11/27	11	3.0	40	44	13	
				39	45	14‡	
	12/ 1	12	3.0	46	38	12	Well; left arm in region of injected site shows tender area indurated about size of a pea
				45	47	7‡	
	12/ 4	13	3.0	54	36	6	Well; left arm same
				45	39	13‡	
	12/ 8	..	...	40	47	10	Well; indurated area on left arm more tender, and skin is slightly red; white blood count, 5,100
	12/11	..	...	42	41	12	Well; left arm unchanged
	12/18	..	...	44	37	16	Well; left arm unchanged
	12/22	..	...	38	39	20	Wheezing on previous day; induration on left arm larger; abscess lanced
	12/27	..	...	55	29	13	Well; slight discharge from wound on left arm
Patient 23, M. B., a boy, aged 12 years; age of onset of asthma, 3 years	4/18/33	..	...	35	56	5	Had grip and attack of asthma five days ago; lungs show residual sibilant râles
	10/26	..	...	34	53	12	Occasional attack of asthma; now is well
	1/25/34	..	...	34	52	10	Well
	10/25	..	...	19	54	24	Wheezing every night at home
	10/27	..	...	31	53	13	Well
	10/30	1	0.5	25	60	12	Well
	11/ 2	2	1.0	32	50	15	Well
	11/ 3	3	1.5	39	40	18	Attack of asthma on previous day
	11/ 6	4	2.0	37	49	11	Well
	11/ 8	5	2.5	37	48	11	Well
	11/10	6	3.0	24	67	4	Temperature 101 F.
	11/13	7	3.0	31	64	4	Well
	11/15	..	...	49	38	9	Well
	11/17	8	3.0	46	43	8	Well
	11/20	9	3.0	69	24	4	Well
	11/22	..	...	51	41	2	Well
	11/24	10	3.0	56	38	2	Well
	11/27	11	3.0	43	47	7	Well
	12/ 1	12	3.0	40	54	5	Well
	12/ 6	..	...	32	57	7	Well

* The basophils and monocytes were omitted for the reason stated in the legend of chart 1.
† A nonreactor by the cutaneous test.
‡ A differential leukocyte count was performed one hour after injection of crotalin solution.

TABLE 1.—*Differential Leukocyte Count for Thirteen Children with Bronchial Asthma Given Injections of Milk with a High Bacterial Count—Continued*

	Date	Number of Injections	Dose in Cc.	Differential Leukocyte Count, Percentage* Polymorphonuclear Neutrophils	Lymphocytes	Eosinophils	Comment
Patient 23, continued	12/ 8	13	3.0	40	44	11	Well
	12/11	..	...	39	40	10	Well
	12/15	..	...	31	55	11	Well
	12/18	..	...	71	21	3	Slight wheezing on previous day
	12/22	..	...	38	51	9	Well
Patient 24, T. W., a girl, aged 7½ years; age of onset of asthma, 5 years†	3/ 9/33	..	...	47	43	7	Attack of asthma on 3/7
	4/13	..	...	33	61	4	Wheezing
	5/25	..	...	40	54	4	Attack of asthma on 5/19
	7/20	..	...	31	54	10	Slight wheezing
	9/ 2	..	...	31	54	6	Occasional coughing only
	10/ 3	..	...	33	58	6	Two attacks last week
	11/28	..	...	35	55	6	Occasional coughing only
	1/11/34	..	...	46	47	7	Attack of asthma on 1/8
	3/22	..	...	66	28	4	Well
	5/31	..	...	49	43	6	Attack of asthma on 5/25
	7/31	..	...	55	35	9	Attack of asthma on 7/28
	9/ 6	..	...	42	45	11	Attack of asthma on 9/2
	10/25	..	...	54	38	5	Well
	10/30	1	0.5	51	40	4	Well
	11/ 1	2	1.0	63	30	2	Well
	11/ 3	3	1.5	48	39	10	Slight wheezing this morning
	11/ 6	4	2.0	51	40	5	Well
	11/ 8	5	2.5	46	40	12	Well
	11/13	6	3.0	43	48	3	Slight cough only
	11/15	7	3.0	50	42	2	Well
	11/17	8	3.0	44	44	9	Well
	11/20	9	3.0	47	44	5	Well
	11/22	..	...	67	23	6	Well
	11/24	10	3.0	63	28	4	Well
	11/27	11	3.0	48	42	5	Well
	12/ 1	12	3.0	49	41	8	Well except for enlarged submaxillary lymph nodes
	12/ 4	..	...	57	33	6	Well
	12/ 8	13	3.0	54	36	6	Wheezing today
	12/11	..	...	48	39	9	Well
	12/15	..	...	48	39	11	Well

* The basophils and monocytes were omitted for the reason stated in the legend of chart 1.
† A nonreactor by the cutaneous test.

POLLEN EXTRACTS

The total number of injections of pollen extracts employed in patients with allergy probably outnumber by far the combined number of injections of all the other antigens used. Thus the importance of pollen antigen in the treatment of the pollen syndrome becomes obvious. The pollen extracts employed in the fourteen patients of this series were prepared after the method of Coca.[6] The number of injections and the doses given to each patient, with the differential leukocyte counts, are set forth in table 2.

6. Coca, A. F.: The Preparation of Fluid Extracts and Solutions for Use in the Diagnosis and Treatment of the Allergies with Notes on the Collection of Pollens, J. Immunol. **7**:163 (March) 1922.

TABLE 2.—*Differential Leukocyte Count for Fourteen Children with Pollen Allergy Given Injections of Specific Pollen Extracts*

	Date	Number of Injections	Pollen Extract Injected, Doses in Cc.		Differential Leukocyte Count, Percentage*			Comment
			Mixed Grasses	Mixed Ragweed	Polymorphonuclear Neutrophils	Lymphocytes	Eosinophils	
Patient 25,				1:50†				
R. R., a girl,	6/ 2/30	13	....	0.05	52	41	4	Well
aged 15 years;	6/ 3	..	....	....	51	43	3	Well
hay fever	6/ 9	14	....	0.08	55	41	4	Well
	8/16	24	....	0.50	54	40	4	Well
	8/17	..	....	....	52	41	4	Well
	9/ 5	26	....	0.50	48	45	3	Moderate hay fever
	9/ 6	..	....	....	54	41	3	Moderate hay fever
Patient 26,				1:5,000				
J. L., a girl,	6/ 2/31	6	....	0.05	44	49	3	Well
aged 12 years;	6/ 3	..	....	....	47	48	3	Well
hay fever	6/ 6	7	....	0.10	41	54	2	Well
				1:50				
	8/15	18	....	0.65	47	48	3	Well
	8/16	..	....	....	45	50	2	Well
	9/ 5	21	....	0.65	48	45	4	Well
	9/ 6	..	....	....	50	44	3	Well
Patient 27,				1:500				
R. C., a girl,	6/ 7/30	8	....	0.03	47	50	1	Well
aged 12 years;	6/ 8	..	....	....	43	53	2	Well
asthma with	6/14	10	....	0.06	41	53	2	Well
hay fever				1:50				
	8/16	20	....	0.80	48	47	1	Well
	9/ 2	22	....	0.80	44	50	3	Well
	9/ 3	..	....	....	46	49	1	Well
Patient 28,			1:50†	1:50				
V. O., a girl,	6/ 2/31	15	0.10	0.07	51	37	10	Slight sneezing for past two nights
aged 13 years;								
asthma with	6/ 3	..	....	....	49	40	8	
hay fever	6/27	21	0.10	0.32	50	40	8	Moderate wheezing in mornings
	6/28	..	....	....	47	51	9	Well
	8/25	31	....	0.64	52	37	10	Well
	8/26	..	....	....	50	37	10	Well
	9/ 8	33	....	0.60	55	38	5	Only an occasional sneeze
	9/ 9	..	....	....	51	39	9	Occasional sneeze
Patient 29,				1:5,000				
M. M., a boy,	5/26/31	12	....	0.15	49	43	4	Well
aged 15 years;	5/27	..	....	....	47	48	3	Well
asthma with	6/ 2	15	....	0.25	50	43	4	Well
hay fever	6/ 3	..	....	....	45	51	2	Well
	6/ 9	17	....	0.60	47	48	2	Well
				1:50				
	8/23	28	....	0.50	49	46	3	Well
	8/24	..	....	....	52	41	4	Well
	9/ 5	30	....	0.50	47	45	4	Well
	9/ 6	..	....	....	49	47	3	Well
Patient 30,				1:500				
M. S., a girl,	5/12/31	13	....	0.45	55	40	4	
aged 10 years;	5/13	..	....	....	52	44	2	
hay fever				1:50				
	6/ 2	16	....	0.11	50	43	3	
	6/ 3	..	....	....	51	44	2	
	7/ 7	21	....	0.20	53	44	1	
	7/ 8	..	....	....	54	40	3	
	9/ 5	31	....	0.50	50	43	4	Slight hay fever
	9/ 6	..	....	....	48	46	4	Slight hay fever
Patient 31,			1:50	1:50				
L. B., a boy,	5/ 5/31	11	0.06	0.04	48	44	6	Well
aged 11 years;	5/16	15	0.12	0.07	40	51	8	Well
hay fever	6/ 2	21	0.50	0.40	46	43	6	Well
	6/ 3	..	....	....	43	48	5	Well
	7/ 7	26	0.50	0.52	49	42	5	Well
	7/ 8	..	....	....	47	44	7	Well
	9/ 5	32	....	0.60	47	45	4	Slight hay fever
	9/ 6	..	....	....	46	44	6	Slight hay fever

* The basophils and monocytes were omitted for the reason stated in the legend of chart 1.
† Figures in boldface type indicate dilution of pollen extract employed.

TABLE 2.—*Differential Leukocyte Count for Fourteen Children with Pollen Allergy Given Injections of Specific Pollen Extracts—Continued*

	Date	Number of Injections	Pollen Extract Injected, Doses in Cc.		Differential Leukocyte Count, Percentage*			Comment
			Mixed Grasses	Mixed Ragweed	Polymorphonuclear Neutrophils	Lymphocytes	Eosinophils	
Patient 32:				1:5,000†				
S. H., a girl,	5/16/31	9	....	0.20	68	23	5	Well
aged 8 years;	5/23	10	....	0.40	66	25	6	Well
asthma and				1:500				
hay fever	6/ 2	12	....	0.06	70	22	5	Coughing
				1:50				
	7/11	18	....	0.14	68	21	6	Slight asthma
	7/12	..	....	....	65	27	6	Slight asthma
	8/22	25	....	0.50	67	27	3	Moderate hay fever
	9/ 5	27	....	0.50	69	23	5	Slight asthma and hay fever
Patient 33,			1:500	1:500				
R. S., a boy,	5/12/31	8	0.30	0.10	54	36	7	
aged 9 years;	5/13	..	....	....	56	36	5	
asthma with	5/19	9	0.30	0.15	63	30	2	
hay fever	6/ 2	12	0.40	0.80	60	33	5	Moderate hay fever
	6/ 3	..	....	....	58	42	6	Moderate hay fever
			1:50	1:50				
	7/ 2	17	0.04	0.18	58	42	6	Slight hay fever
	9/ 5	27	....	0.24	61	33	3	Slight hay fever
	9/ 8	..	....	0.24	64	30	4	Moderate hay fever
Patient 34,			1:50	1:50				
A. H., a boy,	5/12/31	24	0.68	0.38	66	27	3	Well
aged 10 years;	5/13	..	....	....	60	33	4	Well
asthma and	5/16	25	0.72	0.38	64	28	4	Wheezing and slight hay fever
hay fever	6/ 2	29	0.80	0.50	62	30	4	Attack of asthma on 6/1
	6/ 3	..	....	....	58	37	2	Slight wheezing
	7/ 7	36	0.80	0.70	63	36	2	Well
	7/ 8	..	....	....	60	32	4	Well
	9/ 1	43	....	0.76	58	35	2	Very slight hay fever
	9/ 2	..	....	....	64	28	4	Very slight hay fever
Patient 35,			1:500	1:500				
T. S., a boy,	5/16/31	7	0.30	0.10	68	16	12	Very mild asthma
aged 11 years;	6/ 2	10	0.40	0.60	69	17	11	Very mild asthma
asthma and			1:50	1:50				
hay fever	7/ 2	18	0.04	0.34	70	14	12	Very mild asthma
	8/15	25	....	0.50	70	16	9	Well
	8/16	..	....	....	68	22	7	Well
	9/ 5	28	....	0.50	69	18	10	Very mild asthma
	9/19	..	....	0.50	71	13	12	Well
Patient 36,			1:50	1:50				
B. K., a girl,	5/16/31	13	0.24	0.06	57	31	9	Slight hay fever
aged 12 years;	7/ 2	23	0.24	0.28	62	27	7	Slight hay fever
hay fever	8/15	30	....	0.40	55	31	10	Slight hay fever
	9/ 5	33	....	0.40	60	27	8	Slight hay fever
	9/ 6	..	....	....	57	29	10	Well
	9/26	36	....	0.40	61	25	9	Well
Patient 37,			1:50	1:50				
I. G., a boy,	5/19/28	30	....	0.24	34	54	8	Well
aged 10 years;	5/22	31	2.00	....	58	33	5	Well
perennial	5/26	32	....	0.30	32	54	4	Wheezing
asthma‡	5/29	33	2.00	....	37	50	9	Well
	6/ 2	34	....	0.38	37	50	7	Well
	6/ 3	..	....	....	38	48	10	Well
	6/ 5	35	2.00	....	40	45	11	Well
	6/ 6	..	....	....	43	43	10	Well
	6/ 9	36	2.00	0.46	27	60	9	Well
	6/16	37	2.00	0.46	45	45	5	Wheezing
	6/19	38	....	0.56	44	46	5	Attack of asthma
	6/26	39	2.00	0.66	36	54	5	Wheezing
	6/30	..	....	....	49	38	7	Well
	7/ 3	40	2.00	0.76	53	36	7	Well
	7/10	41	....	0.80	43	45	6	Well
	7/17	42	....	0.90	44	46	5	Attack of asthma
	7/24	43	....	1.00	37	52	6	Well
	7/28	..	....	....	65	26	5	Attack of asthma
	7/31	44	....	1.00	50	35	10	Well
	8/12	..	....	....	54	35	7	Attack of asthma

* The basophils and monocytes were omitted for the reason stated in the legend of chart 1.

† Figures in boldface type indicate dilution of pollen extract employed.

‡ These patients gave positive reactions to pollen by the cutaneous test, with a negative history of pollen allergy.

TABLE 2.—*Differential Leukocyte Count for Fourteen Children with Pollen Allergy Given Injections of Specific Pollen Extracts—Continued*

	Date	Number of Injections	Pollen Extract Injected, Doses in Cc.		Differential Leukocyte Count, Percentage*			Comment
			Mixed Grasses	Mixed Ragweed	Polymorphonuclear Neutrophils	Lymphocytes	Eosinophils	
Patient 38,			1:50†	1:50†				
J. B., a boy,	5/29/28	35	0.50	0.14	32	55	9	Attack of asthma
aged 9 years;	6/ 2	36	....	0.18	40	52	5	Attack of asthma
perennial	6/ 4	37	0.45	0.22	52	40	4	Wheezing
asthma‡	6/ 9	38	....	0.25	35	51	10	Well
	6/12	39	0.45	0.28	33	61	2	Well
	6/16	40	....	0.32	37	52	7	Attack of asthma
	6/23	41	0.40	0.36	42	48	5	Wheezing
	6/26	42	....	0.40	47	43	5	Well
	6/30	43	0.40	0.45	23	65	6	Well
	7/ 7	44	0.40	0.50	28	60	8	Attack of asthma
	7/14	45	0.40	0.55	30	58	6	Well
	7/21	46	0.40	0.60	39	50	6	Attack of asthma
	7/28	47	0.40	0.65	35	49	9	Only slight cough
	8/ 4	48	....	0.65	45	44	7	Well
	8/14	49	....	0.65	30	60	5	Attack of asthma

* The basophils and monocytes were omitted for the reason stated in the legend of chart 1.
† Figures in boldface type indicate dilution of pollen extract employed.
‡ These patients gave positive reactions to pollen by the cutaneous test, with a negative history of pollen allergy.

SUMMARY

A summary of the thirty-eight cases comprising this series, with the number of injections, differential leukocyte counts, maximum dosage per patient and other essential details, is given in table 3.

It can be seen from table 3 (also from charts 1 to 11) that the period during which intramuscular injections of venom protein (crotalin) solution were administered averaged approximately one hundred and forty-four days, and the number of injections, about twenty per patient. In the eleven patients the maximum dose of crotalin injected ranged from 0.14 to 1.2 mg., and the total number of differential leukocyte counts was five hundred and nineteen, or an average of forty-seven counts per patient.

All these patients showed an increase in the eosinophil count. The average eosinophil count per patient prior to the injection of crotalin was 6.45 per cent. The maximum count during the course of treatment was 31 per cent, or an average of 19 per cent per patient. The maximum rise in the eosinophil count above the initial level was 21 per cent, or an average of 12.55 per cent per patient.

In four patients (2, 4, 5 and 11) the eosinophil count rose at least 5 per cent above the initial level from one to four days after the first injection of crotalin solution; in two others (1 and 10) the count rose after the second injection; in another two (3 and 6), after the fourth injection, and in the remaining three patients (7, 8 and 9) the eosinophil count did not begin to rise until after the fifth to the eighteenth injection. A rise in the eosinophil count did not necessarily depend on the injection of progressively increasing doses of crotalin solution. A

TABLE 3.—*Summary of Data for Thirty-Eight Children with Allergic Diseases Who Received Injections of Pollen and Nonspecific Antigens with Reference to the Eosinophilic Index* *

Patient	Number of Days Covering Period of Injections†	Number of Injections	Maximum Dose Injected	Number of Differential Leukocyte Counts	Percentage of Eosinophils: Maximum Initial Count	Percentage of Eosinophils: Maximum Subsequent Count	Influence of Injections on the Eosinophil Count: Increased Eosinophilia Followed by Subsequent Return of Eosinophils to Initial or Normal Levels	Influence of Injections on the Eosinophil Count: Relief from Allergic Symptoms as a Result of Treatment
Venon (Crotalin) Protein Solution								
			Mg.					
1	150	23	0.45	67	15	25	No	No
2	123	18	0.14	45	3	21	No	Moderate
3	115	17	0.85	44	3	21	Yes	Marked
4	101	15	0.18	32	10	31	Yes	Marked
5	125	18	0.65	53	8	24	No	No
6	122	18	0.65	37	8	28	Yes	No
7	185	30	1.20	81	6	15	No	No
8	161	23	1.20	57	2	8	Yes	No
9	116	17	1.20	32	6	12	Yes	No
10	105	14	0.18	15	6	12	No	Marked
11	178	25	0.35	56	4	12	No	Marked
Total 11	1,481	218		519				
Milk with High Bacterial Content								
			Cc.					
12	99	14	3	6	2	3	No	No
13	48	11	3	6	9	11	No	No
14	20	9	3	14	3	8	No	No
15	60	13	3	35	6	5	No	Complete
16	52	13	3	20	11	12	No	Moderate
17	60	14	3	35	12	21	No	No
18	62	13	3	16	10	19	No	No
19	56	16	3	30	5	7	No	Marked
20	56	13	3	26	8	6	No	Marked
21	60	14	3	44	16	16	No	Marked
22	63	13	3	40	13	20	No	‡
23	58	13	3	25	24	18	No	Marked
24	51	13	3	30	11	12	No	No
Total 13	745	169		327				
Pollen Extract								
			1:50,§ Cc.					
25	96	26	0.50	7	4	4	No	Moderate
26	96	21	0.65	7	3	4	No	Complete
27	88	22	0.80	6	1	3	No	Complete
28	99	27	0.64	8	10	10	No	Marked
29	103	30	0.50	9	4	4	No	Complete
30	86	31	0.50	8	4	4	No	Moderate
31	124	32	1.02	8	6	7	No	Moderate for ragweed; complete for grasses
32	112	27	0.50	7	5	6	No	No
33	119	27	0.24	8	7	6	No	No
34	113	43	1.50‖	9	3	4	No	Moderate for grasses; marked for ragweed
35	125	28	0.50	7	12	12	No	Moderate
36	133	36	0.52‖	6	9	10	No	Moderate
37	85	44	2.76‖	20	8	11	No	¶
38	77	49	1.05‖	15	9	10	No	¶
Total 14	1,176	374		125				
Grand total 38	3,402	761		971				

* Eosinophilic index is a synonym for eosinophil count.

† This period covers the time during which differential leukocyte counts were made and in some instances includes a period up to about three weeks when counts were made prior to the institution of and after the completion of the course of injections.

‡ No comment on relief from symptoms can be made, since this patient was well prior to the beginning of the injections of milk.

§ Dilution of pollen extract employed.

‖ These antigens given in maximum doses include both grasses and ragweed pollen extracts, which were often injected on the same day.

¶ Patients 37 and 38 showed positive cutaneous reactions to the various grass and ragweed pollens, but the history of pollen intolerance was negative, and perennial asthma was due to other factors. These cases were included to determine the influence of injections of pollen on potentially sensitive persons.

maintained small dose (cases 2, 4 and 10) over varying periods of time also caused a rise in the eosinophil count. Thus, it is evident that with crotalin therapy the most important factor in causing a rise in the number of eosinophils is not the size of the dose but rather the continued administration of the antigen at regular intervals over a definite period of time.

As a result of treatment with crotalin solution there occurred in five patients (3, 4, 6, 8 and 9) the phenomenon of increased eosinophilia followed by a subsequent return of the number of eosinophils to initial or normal levels in spite of continued injections. This is referred to by Spangler [1a] as the phenomenon of nonspecific desensitization, which term is employed in this paper for the sake of brevity and convenience. The maximum dosage of crotalin was required to bring this about in these patients (with the exception of patient 4). Nonspecific desensitization sets in from nine to sixteen weeks after the beginning of treatment.

In some instances, even with small doses of crotalin, there was a temporary aggravation of the asthmatic condition. The influence of the asthmatic attack on the eosinophil count could not be accurately determined because of the possibility of interference of the stimulating influence of crotalin therapy. However, it was of extreme interest to note the influence of intercurrent disease and infection on the eosinophil count during the period of uninterrupted treatment with crotalin solution. Afebrile pertussis (case 1) and grip with elevation of temperature (cases 2 and 7) caused a drop in the eosinophil count to within (a variation of 5 per cent) or near normal levels. The depression in the eosinophil count in the case with pertussis lasted three weeks, while in the patients with grip the count was lowered for shorter periods of time. The eosinophil count was not appreciably disturbed in patients with no fever or only a slight elevation of temperature.

Approximately 45 per cent of the patients treated with crotalin were moderately or markedly relieved from asthma. In three cases (2, 3 and 4) the relief from asthma occurred for two months, two years and four months, respectively. In the other two cases (10 and 11) the injections were continued over a period of eight months and four years, respectively, and relief from symptoms of asthma in the first case occurred for eleven months and in the latter for three and one-half years. Only two of these five patients (3 and 4) showed the so-called phenomenon of nonspecific desensitization. It was also noted that no correlation could be drawn between the percentage of the eosinophils and the absence or presence of asthmatic symptoms. In some instances the patient appeared well in the presence of eosinophilia, and in others asthma was present regardless of the percentage of the eosinophil count.

Crotalin therapy did not afford protection to the patients who acquired pollen allergy.

Sterilized milk with a high bacterial content (tables 1 and 3) was employed for thirteen children each of whom received the maximum dose of 3 cc. The average number of injections per patient was thirteen. The average number of days during which the differential leukocyte counts were made was fifty-seven per patient, and the average number of counts was twenty-five per patient.

Only four patients (14, 17, 18 and 22), approximately 31 per cent, showed a rise of the eosinophil count of at least 5 per cent above the counts recorded prior to the beginning of injections of milk. In this group the average initial eosinophil count was 8.75 per cent per patient. The maximum count recorded during the course of treatment was 21 per cent, or an average of 17 per cent per patient. The maximum rise of the eosinophil count above the initial level was 9 per cent, or an average of 7.5 per cent per patient. The maximum rise in the eosinophil count usually occurred on the second or third day following the injection. In spite of the frequent intervals (from two to three times weekly) that milk was injected, the substantial and sustained rise in the number of eosinophils noted in the patients who were given injections of venom (protein) solution at weekly intervals was lacking.

Differential leukocyte counts were made immediately before and one hour after the injection of milk in four cases (15, 17, 21 and 22). At the end of one hour there was a rise in the eosinophil count in twenty-two instances and a decline in nineteen for an average of 1.8 and 3.2 per cent, respectively, per instance. In nine instances no change occurred in the eosinophil count.

The clinical condition of the patient and the dose or the number of injections administered bore no relationship to any of these counts. The so-called phenomenon of nonspecific desensitization did not occur in a single patient.

In two instances (cases 16 and 18), in which the patients were insensitive to milk, anaphylactoid shock immediately followed the injection of milk. This type of shock is differentiated from the general shock following a specific antigen only in that the former is readily controlled with one injection of epinephrine hydrochloride (a 1 : 1,000 solution), with no recurrence of symptoms. One of the patients (18) had an elevation of temperature several hours after the injections.

Acute rhinitis in one patient (22), with a negligible rise in temperature (to 100 F.), caused no depression in the eosinophil count. In another patient (23) who had an unaccountable elevation of temperature (to 101 F.) the eosinophil count was lowered for four days from 11 to 4 per cent.

Moderate to marked relief from asthma resulting from milk therapy occurred in six patients, or 50 per cent of the cases (only twelve cases were recorded for this tabulation [table 3]). The relief from symptoms

was only temporary, and the periods of relief were of shorter duration than that afforded by crotalin therapy.

Thirteen children (tables 2 and 3) were given injections of pollen extracts, the maximum dose ranging from 0.5 to 2.76 cc. of a 1:50 dilution of extract, with the exception of one child who received a maximum dose of 0.24 cc. The average number of injections per patient was twenty-seven, and the period of time during which the differential leukocyte counts were made averaged eighty-four days per patient.

The eosinophil count was not raised above the normal range of oscillation in a single case. It did not seem to matter whether the counts were begun early or late in the course of pollen treatment.

Vallery-Radot and his collaborators [7] reported that the eosinophil count was normal in the preseasonal period and raised during the period of active symptoms in patients with hay fever, while Sternberg [8] stated that patients successfully treated with pollen extract have mostly a normal eosinophil count during the pollen season. In our series of cases there did not appear to be any correlation between the percentage of eosinophils and the absence or presence of symptoms of pollen allergy.

The phenomenon of specific desensitization was not observed to occur.

Moderate to complete relief from symptoms of pollen allergy occurred in ten of twelve patients (cases 37 and 38 are not included for the reasons stated in table 3), an incidence of 83 per cent.

The influence of pollen, crotalin and milk on the polymorphonuclears, lymphocytes, monocytes and basophils was nil. The usual relationship between the polymorphonuclear and lymphocyte curves was observed. When the former curve was raised the latter was lowered, and vice versa. A raised eosinophil curve did not always occur at the expense of the polymorphonuclears. During an infection when the esosinophil cells dropped to within normal levels the monocytes were seen to rise and in one instance increased up to 10 per cent.

COMMENT

Eosinophilia in animals has been brought about experimentally by the injection of a variety of protein substances.[9] Moreover, it has been

7. Vallery-Radot, P.; Blamoutier, P.; Claude, F., and Giroud, P.: Blood Eosinophilia in Anaphylactic Conditions, Presse méd. **34**:1601 (Dec. 22) 1926.

8. Sternberg, L.: Eosinophilia in Hay Fever, Am. J. M. Sc. **176**:82 (July) 1928.

9. Schlecht, H., and Schwenker, G.: Ueber locale Eosinophilie in den Bronchien und der Lunge beim anaphylaktischen Meerschweinchen, Arch. f. exper. Path. u. Pharmacol. **68**:163, 1912; Ueber die Beziehungen der Eosinophilie zur Anaphylaxie, Deutsches Arch. f. klin. Med. **108**:405, 1912. Weinberg, M., and Seguin, P.: Propriétés phagocytaires de l'éosinophile: Absorption de l'antigène hydatique par les éosinophiles démontrée par la réaction de fixation, Compt. rend. Soc. de biol. **76**:715, 1914.

shown by Biggart,[10] Hajos and Mazgon [11] and others that eosinophilia follows repeated injections of large doses of an antigenic substance—specific or nonspecific—and not after the first injection or after repeated small doses. With the large doses of antigen the rise in the number of eosinophils occurs in twenty-four hours. The eosinophil count falls during the second day, but the percentage still remains at a higher level than previously. Each injection seems to produce a progressive effect, which was also reported by Herrick [12] and others. In experimental anaphylaxis local and general eosinophilia can be demonstrated only during the stage of antianaphylaxis.[13]

In patients with asthma Spoujitch [14] found that after numerous repeated injections of horse serum the number of eosinophil cells showed no noticeable change, although local reactions as well as hemoclastic crisis followed the injections. Injections of milk in doses sufficiently large to cause shock produced a slight increase in the eosinophil count only during the period of shock. Schlecht,[15] however, reported an increase of eosinophil cells after an injection of foreign protein such as horse serum. Peipers [16] injected various specific allergens in certain groups of allergic and normal persons, while Sternberg [8] injected pollen extract; both were unable to demonstrate an increase in the number of eosinophil cells. Baagøe [17] stated that the age of the child does not seem to play an essential part with regard to the number of eosinophils. In normal children aged from 3 to 14 years the number of eosinophils vary considerably, but the percentage most frequently found was approximately 3. Spangler,[1] who worked with venom protein solution, considers the eosinophil count (eosinophilic index) an important guide in determining the degree of hypersensitivity of a patient and in regulat-

10. Biggart, J. H.: Some Observations on Eosinophile Cell, J. Path. & Bact. **35**:799 (Sept.) 1932.

11. Hajos, K., and Mazgon, R.: Eosinophilia During Desensitization, Ztschr. f. d. ges. exper. Med. **68**:767, 1929.

12. Herrick, W. W.: Experimental Eosinophilia with an Extract of an Animal Parasite, Arch. Int. Med. **11**:165 (Feb.) 1913.

13. Hajos, K.: Distribution of Eosinophil Cells After Protein Injection and Induced Anaphylaxis in Guinea-Pigs, Ztschr. f. d. ges. exper. Med. **59**:383, 1928.

14. Spoujitch, V.: Eosinophilia After Injections of Foreign Protein and in Hemoclastic Shock, J. de physiol. et de path. gén. **26**:655 (Dec.) 1928.

15. Schlecht, H.: Ueber experimentelle Eosinophilie nach parenteraler Zufuhr von artfremdem Eiweiss, und über Beziehungen der Eosinophilie zur Anaphylaxie, Arch. f. exper. Path. u. Pharmakol. **67**:138, 1912; Ueber die Einwirkung von Seruminjektionen auf die Eosinopilen und Mastzellen des menschlichen und tierischen Blutes, Deutsches Arch. f. klin. Med. **98**:308, 1910.

16. Peipers, A.: Eosinophilia und Allergie: Klinisch-experimentelle Untersuchungen über ihre Beziehungen, Deutsches Arch. f. klin. Med. **169**:65, 1930.

17. Baagøe, K. H.: Eosinophil Cells in Blood of Normal and of Asthmatic Children, Am. J. Dis. Child. **35**:171 (Feb.) 1928.

ing the dosage and frequency of administration of nonspecific agents in desensitization treatment. Van Leeuwen and van Niekerk [18] found that the relief of allergic symptoms in man does not seem to be bound up with the fall in the number of eosinophils.

In view of all of the foregoing findings it becomes evident that the response of the eosinophil cells to various antigenic substances in the animal is in marked contrast to the lack of uniformity of response in man. The answer to this variability of eosinophilic response in man may be found in one or any combination of the following: the particular antigenic substance employed, the number of injections, the dose and the protein content of the antigen. Of clinical interest also and requiring solution is the question whether or not the return of an elevated eosinophil count occurring during the course of injections with antigenic substances to the level before injection or the normal level is an indication of the so-called phenomenon of nonspecific or specific desensitization. The following considerations are submitted in explanation.

An approximation of the protein content of the maximum doses of the antigenic substances—venom protein solution, milk with a high bacterial content and pollen extract—employed in this study is as follows: The maximum dose of the naturally dried crystals of Crotalus horridus or Crotalus atrox was 1.2 mg., and the protein content is considerably less. Three cubic centimeters (48 minims) of cow's milk, not taking into account the bacterial content, contain 106 mg. (1½ grains) of protein. The total nitrogen content of 2.76 cc. of a 1:50 dilution of pollen extract (1 cc. contains roughly 0.4 mg. of total nitrogen for ragweed and grass pollen extracts) is about 1.1 mg., and the protein nitrogen content is about 0.6 mg.[19] Crotalin had the power to raise the eosinophil count in all patients who received injections, milk in 31 per cent of the cases and pollen in no case. It is apparent from the clinical facts and from all the foregoing figures that essentially it is the particular antigen employed rather than the protein content of the antigen that is the stimulating factor in causing a rise in the eosinophil count. A study of the various tables and charts in this series shows that in the patients given injections of pollen extract the number of injections or the strength of the dose had no influence on the eosinophilic index. Moreover, some of the patients who received injections of venom protein solution did not begin to respond with an increase in the eosinophils until after repeated injections of a stationary dose or an increasing dose was given. If the eosinophil cell is accepted as playing an important

18. van Leeuwen, S., and van Niekerk, J.: Eosinophilia in Allergic Persons, Ztschr. f. d. ges. exper. Med. **63**:393, 1928.

19. Stull, A.; Cooke, R. A., and Tennant, J.: The Allergen Content of Pollen Extracts: Its Determination and Its Deterioration, J. Allergy **4**:455 (Sept.) 1933.

part in the defense mechanism of the body and when one takes into account the higher incidence of therapeutic results brought about by a specific antigen like pollen (with its lack of influence on the eosinophil cell as compared to antigens like milk and venom protein solution), it seems reasonable to assume that the absence of an increase in the eosinophil count following the injection of an antigenic substance is no indication that the "defense mechanism" is not brought into play.

The occurrence of a condition in which eosinophilia is changed to eosinopenia or to a normal eosinophil count during the course of pertussis and febrile infections, in spite of the continued injection of an antigen, seems to be due to the depressing influence of the intervening disease on the eosinophil cell. These infections appear to overwhelm the stimulating influence of the antigenic substance on the eosinophil cell. This phenomenon should not be confused with the so-called nonspecific desensitization that may occur following repeated inoculations of venom protein solution independent of intercurrent infection. The occurrence of so-called nonspecific desensitization, with a return of the eosinophil count to normal levels in a patient free from asthma, should be considered for the present as indicating a state of freedom from allergic symptoms rather than a state of nonspecific desensitization per se. Baagøe [17] and others have shown that when children are freed from asthmatic symptoms soon after hospitalization they frequently demonstrate a drop in the eosinophil count to normal levels. It does not seem plausible to assume that either hospitalization or injections of antigenic substances possess the power to alter a constitutional or general body tissue sensitivity and that a return of the eosinophil count to normal levels is an indication of such alteration. It should be emphasized that patients who are entirely free from allergic symptoms too frequently have eosinophilia.

From the present study no definite significance could be justifiably attached to the varying percentage of the eosinophil cells during various stages of asthma and hay fever, nor could a proportional rise in the eosinophil count following an injection or injections of venom protein solution or milk be employed as a reliable guide to the regulation of the dosage or the frequency of administration of these nonspecific agents. The safe and practical guide employed by most allergists is as follows: An increase in the dose of the antigenic substance may be administered when the previous dose caused no immediate or delayed general reaction along with a minor or no local reaction at the site of the injection.

CONCLUSIONS

1. A detailed study on the differential leukocyte count with special reference to the eosinophils has been presented. It was based on findings

for thirty-eight ambulant children suffering from asthma or hay fever. The influence of the injections of venom (Crotalus horridus and Crotalus atrox) protein solution, sterilized skimmed milk with a high bacterial content and extracts of pollen was noted.

2. The influence of the injection of antigenic substances on the cells of the blood other than the eosinophils was nil.

3. Crotalin caused an appreciable increase in the eosinophil cell in the eleven patients given injections of this antigen. The maximum dose of crotalin ranged up to 1.2 mg. The average maximum eosinophil count per patient prior to treatment by injection was 6.45 per cent. The average maximum count during the course of treatment was 19 per cent per patient, while the highest count for any one patient was 31 per cent.

Milk caused an appreciable increase in the eosinophil cell in only four of the thirteen patients given injections of this antigen. The maximum dose of milk in each case was 3 cc.. The average maximum eosinophil count per patient prior to treatment by injection was 10 per cent. The average count during the course of treatment was 12 per cent, while the highest count reached by any one patient was 21 per cent.

Pollen did not cause an appreciable increase in the number of eosinophil cells in any one of the fourteen patients who were given injections of this antigen. The maximum dose ranged up to 2.76 cc. of a 1 : 50 dilution of pollen extract. The average maximum eosinophil count per patient during the early stages of treatment was 6 per cent. The average maximum count during the periods of maximum dosage was 6.7 per cent, while the highest count reached by any one patient was 12 per cent. Thus, the stimulating influence of antigenic substances on the eosinophil cells in man seems to be essentially bound up with the particular antigen employed rather than the dose or the number of injections administered.

4. Five of the eleven patients treated with venom protein solution showed during the course of treatment (and despite continued injections) the phenomenon of increased eosinophilia followed by a subsequent return of the eosinophils to the levels before injection or the normal levels. This has been referred to as nonspecific desensitization.[1b]

The implication that certain oscillations in the percentage of the eosinophil cell count brought about by the injection of an antigen such as crotalin can serve as an indication of an actual alteration of a general body tissue sensitivity cannot be based on the data at hand. No correlation could even be drawn between the occurrence of nonspecific desensitization and the degree of relief from asthmatic symptoms. Besides, none of the patients treated with the nonspecific milk and specific pollen antigens showed the so-called phenomenon of nonspecific desensitization.

5. The stimulating influence of crotalin and milk antigens on the eosinophil cell is nullified by pertussis and febrile grip. The depression of the eosinophil count to below the normal level is maintained mostly during the height of these infections and despite the continuance of treatment by injection. There is every reason to believe that the eosinophil count under the influence of nonspecific antigens would show similar changes in febrile diseases other than grip.

The eosinophil count is not appreciably disturbed in patients with respiratory infections which cause no or only negligible elevation of temperature.

6. No parallelism occurred between the presence or absence of stimulation of the eosinophil cells and the results of treatment by injection with the antigens employed. The degree of relief from allergic symptoms in the patients treated with crotalin, milk and pollen antigens was 45, 50 and 83 per cent, respectively. The relief was marked and more lasting in the patients treated with specific pollen extracts and least and of shortest duration in those treated with the nonspecific milk antigen. These figures are of interest when one considers the fact that venom (crotalin) protein has the most stimulating influence on the eosinophil cell, yet crotalin therapy is no more effective than milk therapy, and both are much less effective than specific pollen therapy.

7. The rôle of the eosinophil in allergic conditions is a question for further intensive investigation. The significance of the eosinophil cell is still unknown.

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GASTRIC ASPIRATION IN CHILDREN WITH PNEUMONIA TO OBTAIN MATERIAL FOR PNEUMOCOCCUS TYPING

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Pulmonary inflammation is usually associated with increased pulmonary secretion. Even in the absence of cough this secretion is carried by peristalsis and ciliary action to the rima glottidis, whence it overflows into the gastro-intestinal tract. In the acid contents of the stomach the mucus is not dissolved.

Gastric lavage has been successfully used on children in examining the contents of the stomach for tubercle bacilli. By gastric aspiration we have extracted with an alternating vacuum the contents of the stomachs of fasting infants and children for the purpose of typing, though with gastric lavage we were unsuccessful. The method is as follows:

For gastric aspiration there are required: a 50 cm. tube, 4 mm. in diameter, with a 2 mm. bore; a 20 cc. Luer syringe; a Petri dish; 10 cc. of distilled water, and typing serums for the several types of pneumococci.

The child is wrapped in a mummy bandage, and the tube is introduced into the stomach. The length of tubing to be introduced is determined approximately by the distance from the root of the nose to the ensiform process of the sternum. After introduction, suction is applied with the syringe. If the thick mucoid secretion is not seen to enter the syringe, as usually happens, an alternating vacuum is created by repeated partial withdrawing of its piston. With a vacuum in the syringe to retain any mucus adherent to the opening or to extract any mucus in the esophagus, the small rubber tube is withdrawn. The end of the tube is then placed in a test tube containing 10 cc. of sterile saline solution so that the mucus in the tube may be flushed into the syringe. The tube is then detached, and both mucus and saline solution are discharged into a Petri dish. Flecks of mucus are then examined directly, the Neufeld swelling reaction being employed. One cubic centimeter of the most mucoid portions may be collected in a syringe for injection into a mouse, or the entire contents may be centrifugated and the sediment injected. In children without respiratory infections no flecks of mucus are seen, and from them no growth is obtained after injection of the sediment into a mouse. The results on twenty-two children and on five controls are given in table 1.

This research received financial support from the Metropolitan Life Insurance Company.

From the Littauer Pneumonia Research Fund of New York University, and the Medical Service, Harlem Hospital (Department of Hospitals).

It will be seen that this method was very satisfactory, with a high incidence of success in obtaining pneumococci of a definite type; it more frequently gave satisfactory results than laryngeal and pharyngeal swabs, and in some cases, especially cases of bronchopneumonia, it was more satisfactory than aspiration of lung tissue by transthoracic pulmonary suction. The other methods employed for infants and small children, who rarely expectorate, are as follows:

1. Incubation of the throat swabs in broth for three hours and then injection of the broth into a mouse. Occasionally, mucus has been obtained on an applicator of cotton by swabbing the larynx or by placing the applicator in the path-

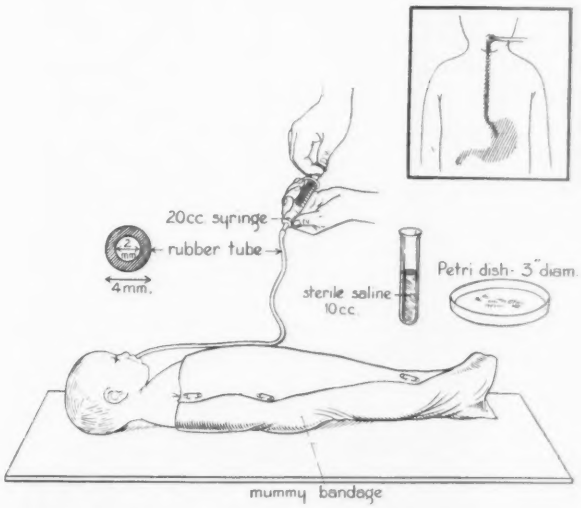

Chart showing the method used for gastric aspiration in children with pneumonia to obtain material for pneumococcus typing.

way of the expiratory blast after irritation has produced a cough. This may be done either with or without the assistance of direct laryngoscopic observation. The mucus may be cultured in broth or directly typed.

2. Study of the secretion obtained from the lung by transthoracic pulmonary puncture, either directly or after incubation in broth.

This method of gastric aspiration has definite advantages: 1. It requires less manipulative skill and is less disturbing to the patient than the laryngoscopic examination. 2. It may be repeated several times. Repetition is undesirable in the case of pulmonary suction. 3. It may be used in cases in which the physical signs are not definite. It is also useful in instances of scattered pneumonia in which the tip of the needle may not strike a diseased area. In all cases diagnostic information concerning the character and amount of pulmonary secretion is supplied. In only one case in the present series did it give misleading

TABLE 1.—*Results of Gastric Aspirations Made on Infants and Young Children with Pneumonia and on Controls for the Purpose of Typing of Pneumococci*

Name of Patient	Age	Length of Illness, Days	Location of Lesion: Physical	Location of Lesion: Roentgenologic	Termination or Complication	Type of Pneumococcus*: Pharyngeal Swab†: Peritoneal Puncture	Type of Pneumococcus*: Pharyngeal Swab†: Injection into Heart of Mouse	Type of Pneumococcus*: Pulmonary Suction	Gastric Aspiration†: Direct Neufeld Reaction	Gastric Aspiration†: Injection into Peritoneum or Heart of Mouse
E. M.	12 mo.	10	L.U.L., L.L.L.	L.U.L., tuberculous tracheal and bronchial lymph nodes	Transferred to Seaview Hospital for Tuberculosis	0	6	None	Not done	6
C. R.	11 mo.	11	R.U.L.	R.U.L.	Cured	Staph. albus, Str. gamma	Bacilli	Not done	14	14
G. J. R. J.	10 wk.	7	L.L.L.	L.L.L.	Cured	0	Staph., Str.	9	Not done	9
C. K.	10 mo.	9	R.U.L., R.M.L.	R.U.L.	Cured	0	Staph., Str.	No growth	Staph., Str., D. pneumoniae	14
M. B.	18 mo.	7	R.U.L., R.L.L.	R.U.L., R.L.L., L.L.L.	Died	Str. alpha	Str. alpha	No growth	0	20
J. V.	2½ yr.	5	L.L.L.	L.L.L.	Cured	Str.	14	No growth	14	14
E. R.	16 mo.	7	L.L.L.	L.L.L.	Cured	Str.	14	No growth	14	14
B. H.	9 yr.	3	R.L.L.	R.L.L.	Cured	Not done	Str.	Not done	Too few organisms	Str.
R. W.	6 mo.	5	L.L.L.	L.L.L.	Cured	.....	D. pneumoniae, Staph.	14	Not done	14
A. U.	2 yr.	11	R.L.L.	R.L.L.	Unresolved pneumonia	0	0	14	D. pneumoniae	14
T. I.	6 mo.	?	R.L.L., R.M.L.	R.L.L., R.M.L., thick pleura	Cured	D. pneumoniae	Bacilli	Not done	0	32
E. S.	7 mo.	12	R.L.L.	.....	Cured	0	3	3	0	3
R. R.	3 yr.	5	R.L.L.	R.L.L.	Empyema type I, cured	0	17	No growth	Not done	17
A. D.	4 yr.	7	R.L.L.	Bronchopneumonia	Cured	14	14	14	14	14
J. B.	1 yr.	9	R.L.L.	R.M.L.	Cured	0	1	Not done	Not done	1
J. C.	17 mo.	10	R.U.L.	Bronchopneumonia	Cured	0	Str., Staph.	No growth	Not done	6
R. S.	18 mo.	12	R.M.L., R.L.L.	R.L.L.	Cured	Staph. albus	Staph. albus	Bacilli (contaminated)	Not done	14
W. S.	14 mo.	14	Bronchopneumonia	Bronchopneumonia	Cured	6	6	Not done	Not done	6
D. J.	15 mo.	5	Bronchopneumonia	Bronchopneumonia	Cured	Not done	Str., Staph.	Not done	0	8
L. J.	16 mo.	6	Bronchopneumonia	Bronchopneumonia	Rickets; cured	0	19	Not done	19	19
B. C.	2 yr.	8	Bronchopneumonia	None	Cured	Bacilli, D. pneumoniae, Str.	24	Not done	D. pneumoniae	24
F. C.	11 mo.	5	Bronchopneumonia	Bronchopneumonia	Protracted course	0	Staph. albus	Not done	0	Staph. albus
I. T.	3 yr.	7	Acute bronchitis	None	Cured	0	19	Not done	19	..

Name of Control	Diagnosis	Gastric Aspiration
A. J.	Hernia	No mucus, no growth in mouse
H. J.	Hernia	No mucus, no growth in mouse
G. C.	Boarder baby (mother ill)	No mucus, no growth in mouse
H.	Hernia	No mucus, no growth in mouse
F. L.	Hernia	No mucus, no growth in mouse

* In six of fifteen cases in which the direct or Neufeld examination was attempted, it was impossible to obtain the type, though it was found later by injecting the broth into a mouse and using the Sabin technic. These successive gastric aspirations were performed by Dr. Wittes. Until skill is acquired by those attempting the method, the results may be less satisfactory. The abbreviations used are: L.U.L., left upper lobe; L.L.L., left lower lobe; R.U.L., right upper lobe; R.M.L., right middle lobe; R.L.L., right lower lobe.

† Staph. indicates staphylococcus; Str., streptococcus, and D., diplococcus.

information, which could have been corrected by another and more successful pulmonary suction; this was the case in which the type I pneumococcus was responsible for the empyema. The type XVII pneumococcus was obtained from the pharynx and by gastric aspiration. It may have been present in the nasopharynx, or it may have been a coinvader of the lung with the type I organism. The cases are summarized in table 2.

TABLE 2.—*Methods of Obtaining Mucus for Typing of Pneumococci from Infants and Young Children with Pneumonia* *

	Throat Swab		Pulmonary Suction		Gastric Aspiration	
Result of Culture	Lobar Pneumonia, Cases	Bronchopneumonia (8) Bronchitis (1) Cases	Lobar Pneumonia, Cases	Bronchopneumonia, Cases	Lobar Pneumonia, Cases	Bronchopneumonia, Cases
Etiologic organism obtained	8	5	5	1	15	8
Etiologic organism not obtained	7	4	6	1	0	1
Culture not done	0	0	4	7	0	0
Total	15	9	15	9	15	9

* The patients were studied in the Pediatric Service at Harlem Hospital through permission of Dr. Morris Gleich.

SUMMARY

Gastric aspiration of the pulmonary secretion of infants and young children suffering from pneumonia is a satisfactory method for determining the type of pneumococcus responsible for the disease.

PLOTTING OF A GRAPHIC RECORD OF GROWTH FOR CHILDREN AGED FROM ONE TO NINETEEN YEARS

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AND
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Physicians, parents and children are frequently interested in determining the relation of the size of a child to the normal. It may be recalled that there are at least three ways of doing this. As an example, the evaluation of the height of a child may be considered.

A first step is to estimate from the comparison of the heights of the parents with that of the average adult how much variation from the normal height should be accepted for the child. The defect in this method is that the law of heredity is not sufficiently understood to make such a prediction possible. The best method that can be proposed is a rough approximation based on the expectation that the stature of the child at maturity will be an average of the values for the parents. To use this method, the stature of the parent of the sex opposite that of the child must first be converted by a factor into the appropriate stature for the other sex. Pearson [1] stated: "Practically it is enough to add $\frac{1}{12}$ to the stature of a woman to convert it into the male equivalent and to take $\frac{1}{13}$ from a man's stature to reduce it to the female equivalent."

Second, the stature may be compared with the average value for a person of the appropriate age, taken from a table. This method, unfortunately, gives no explicit idea of the extent to which the height of the child varies from the expected value.

Third, the stature may be plotted year by year and the curve inspected merely to see whether the annual increase is reasonably satisfactory, i. e., roughly 5 cm. or 2 inches a year.

Fourth, one may use a combination of the second and third methods, and this is done in the chart for the recording of growth presented in this paper. This chart permits also the consideration of height and weight simultaneously, thus giving at one time an evaluation of growth in the two main dimensions.

From the Department of Medicine of the Stanford University School of Medicine.

1. Pearson, Karl: On a New Theory of Progressive Evolution, Ann. Eugenics **4**:1 (April) 1930.

For infants there is Faber's [2] graph for recording weights, which has the merits of easy reading and parallel metric and English scales and especially of emphasis on the representation of normal values as a zone rather than a line. With this as a basis, we have prepared a graph for children of each sex from the age of 1 year on, in which, however, not only weight but height may be recorded and in which a normal zone is indicated for each dimension. This translation of the common standards for height, weight and age from table to graph seeks to provide a simple visual record in which the growth of a child may be seen as a progressive process related not only to the normal value for that moment but to his own developmental tendency. The actual charts for use are 7¼ by 10¾ inches, printed on regular ledger paper 8½ by 11 inches.

CONSTRUCTION OF CHART

Stature is found on the vertical axis and weight on the horizontal, and both axes are calibrated in the metric and English scales. The normal range of height for each age is shown by the vertical bars, and the normal range of weight for height, by the open stream. The height and weight of the child at any one time are plotted as a single small circle. The graph indicating the normal range of values for boys aged from 1 to 19 is shown in chart 1.

The materials used as the basis of the study chart were the values obtained for private school children published by Gray and Ayres,[3] supplemented by further calculations from their original record sheets. These children might seem to form too selected a group, but they are considered suitable because (1) they were born in the United States of northwestern European stock, (2) they were brought up under the best available conditions, (3) the selection and average build were approximately the same as those of the children in the series of Baldwin and (4) there is the further asset that other traits have been measured for these children and reported together with their desirable statistical variabilities.

The construction of the charts is as follows: The average height and weight for each age are shown by a solid dot with the age indicated beside it. Each vertical bar represents a variation of height for age (expressed in the same units as the average values, i. e., centimeters or inches) of plus or minus twice the standard deviation ($\pm 2\ \sigma$), that is, the range which is expected by chance to include 96 per cent of normal children of race and environmental advantages similar to those of the children from whom data for the diagram were derived.

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2. Faber, H. K.: A New Form of Weight Chart for Infants, California State J. Med. **18**:225 (June) 1920.

3. Gray, H., and Ayres, J. G.: Growth in Private School Children, Chicago, University of Chicago Press, 1931.

The expected deviations of weight for height are shown by the open stream, which is delimited by two smoothed curves through points representing values of plus or minus twice the standard deviation of weight for children of several statures.

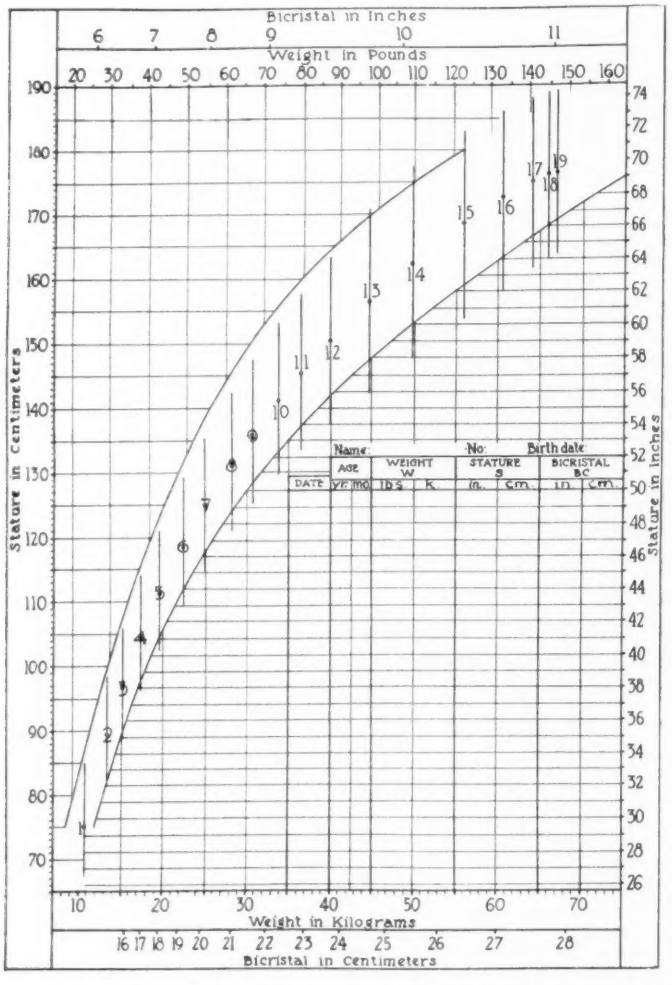

Chart 1.—Graph showing range of values for height and weight for boys of from 1 to 19 years.

Since satisfactory standard deviations of weight for height were not found, they were computed from the original observations at seven levels of stature for boys and five for girls. Incidentally, the average weights for height, calculated simultaneously and plotted (but not reproduced), were found to form a curve very close to that of the solid dots shown for the average height and weight for each age.

Percentage Deviation.—In order to relate the present graphic standards of normal variation to the percentage deviation so frequently used, we calculated the average percentage variability for measurements represented by our charts. Since the standards for both height and weight are based on a range including plus or minus twice the standard deviation ($\pm 2\sigma$), their percentage variability is twice the coefficient of variation ($CV = 100\,\sigma/_{m}$). The coefficients of variation were therefore calculated, doubled and averaged. The following values were obtained for the average percentage variability for height and weight:

	Boys	Girls
Stature	8.4	8.1
Weight	20.4	23.6

Or, if one states it differently, the chart is planned on the expectation that the stature of 96 per cent of normal boys and girls will fall within 8 per cent above or below the average height for the age, and the weight within plus or minus 20 per cent for boys and 24 per cent for girls. If these variabilities for weight seem surprisingly wide, it should be recalled that according to the curve for normal probability 68 per cent of the normal values are expected to fall within a range of once the standard deviation above or below the average, which is equivalent on the charts to a deviation of only about 10 per cent for boys and of 12 per cent for girls. Nevertheless, it seemed wise to plan the charts to include the larger variability, because this more nearly represents permissible biologic variation.

COMMENT

Clinical Significance.—For children of each age represented the average height and weight can be read from the dot numeral directly to the margin.

For the particular child in the office, the plotted circle for stature and weight offers immediately to the eye an answer to the question: "Are the height and the weight normal?" When both values are normal, the plotted circle will lie within the stream, somewhere between the upper and the lower end of the vertical bar marked with the child's age. For instance, the circle for a girl near her eighth birthday should lie within the shaded area shown in chart 2.

The position of the circle for the child may be assessed more accurately by the following considerations: The significance of a circle for height and that for weight must now be analyzed separately. Its meaning for stature is determined by considering its position on the vertical axis as compared with the bar representing the average height for the age of the child at the time the circle was plotted; its meaning for weight depends on its horizontal position in the open stream. To be more specific, we may amplify as follows:

For determination of height, the circle is referred to the bar corresponding to the age of the child (at his nearest birthday), even though several bars may intervene between the circle and the appropriate bar. For instance, the circle for a child who is tall for his age may fall in a

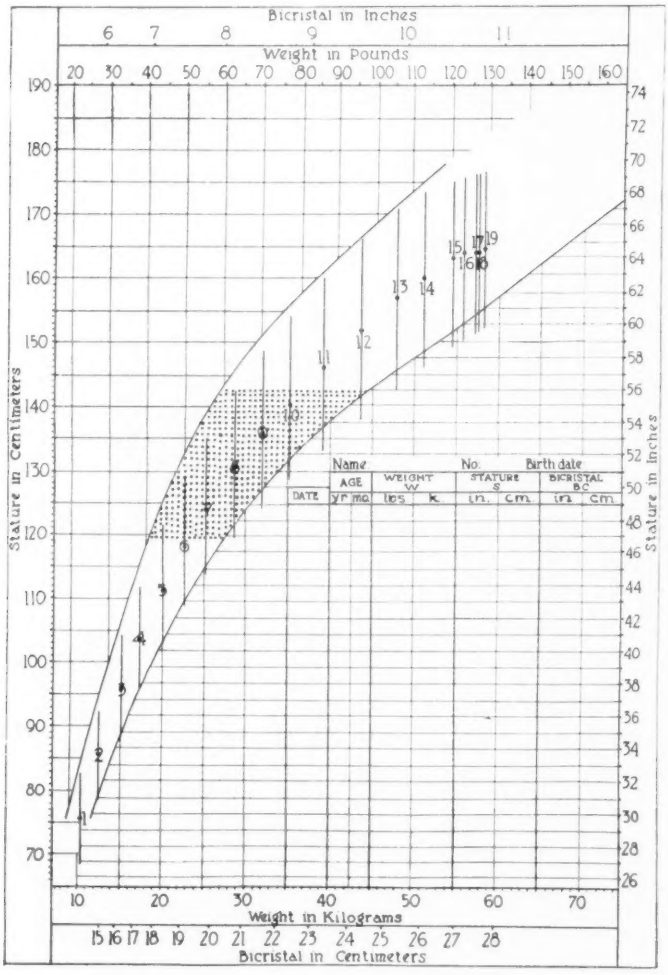

Chart 2.—Graph showing the zone of normal values for height and weight for an 8 year old girl.

spot which is separated by as much as two height bars from his own. This is true because the horizontal position of a point is determined by weight, irrespective of height.

For determination of weight, on the other hand, the circle is to be judged with respect to its position in the open area, whether it is toward the right or toward the left of the stream. Values for stocky children

will be plotted toward the right border and those for slender ones toward the left; values for frankly obese children will be plotted outside the border to the right and those for extremely thin ones outside on the left.

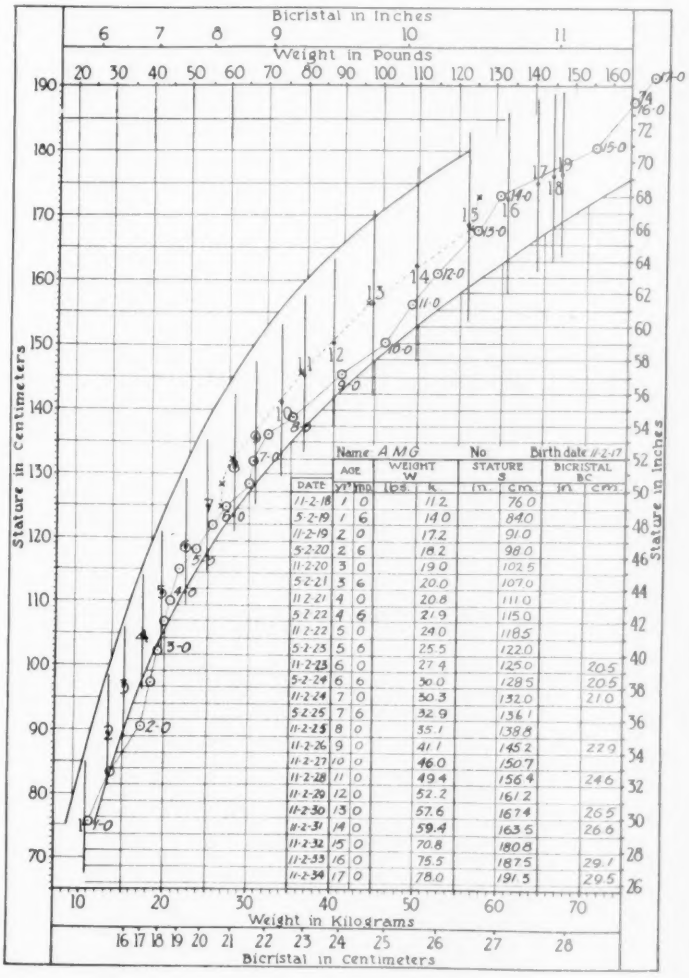

Chart 3.—Graph for a very tall, well nourished boy. The plot for height shows that at the age of 2 years the boy was of average stature but that since that time he had grown always relatively taller: At the age of 7 his height was at the level of that for an average boy of 8; at 10, at that for a boy of 12, etc. It remained, however, within the expected variation for his age until the time of plotting the last circle, when at the age of 17 he was taller than 96 per cent of boys of 17 and even of 19. The curve for weight shows that the boy was somewhat heavy, being definitely overweight between the ages of 1½ and 3 years, but that the position of the circles for weight approached the middle of the stream in adolescence. The crosses for bicristal diameter show that the bony breadth was about that of the average throughout the period of observation.

The curve for growth which results from plotting a series of circles at appropriate time intervals is, of course, to be similarly interpreted. The growth of the child in stature is determined by scrutinizing each circle separately, but the tendency to be slender or stout can be seen at a glance by the position of the whole curve.

Bicristal Diameter.—It may be desired to compare the actual weight with the weight predicted on the basis of still a third criterion, namely, a measure of bony body width, such as the bicristal diameter, as several students have recommended.[4] For this the graph makes provision. Adjacent to the horizontal scales for weight are placed scales for bicristal diameter so arranged that the average bicristal diameter for each age represented coincides with the average weight for that age. In order to make the averages for the two measurements coincide it was necessary to graduate the scales for bicristal diameter unevenly, but since each stroke represents either 1 inch or 1 cm., the nonuniform scale causes no difficulty in plotting. Furthermore, when plotted against these scales the standard deviation for bicristal diameter as calculated for each age roughly coincides with that for weight, and therefore the open area can be assumed to have roughly the same significance for bicristal diameter that it has for weight.

In practice, therefore, to determine how the actual weight of a child compares with his weight predicted on the two factors of stature and bicristal diameter, one may plot, besides the usual circle for weight in relation to stature, a cross for bicristal diameter in relation to stature. If the build is normal, the cross is expected to lie near the circle or not distant by more than about half the width of the open area. But if, for example, the cross lies near the left border of the stream while the circle lies near the right (even though both are thus within the limits for normal values), the weight is to be considered as probably too high for the bony build.

In passing, it should be pointed out that for very plump children the bicristal diameter can be used only with reservations as a criterion of build, because when there is much fat over the bony eminences this measurement may lose its value for the prediction of weight, as was shown for the diameter of the chest by Root and Miles.[5] Perhaps the critical use of a chart such as this can help evaluate the worth of the bicristal diameter in the prediction of weight.

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4. Gray, H.: The Relation of Weight to Suture, Bi-Cristal Diameter and Age, Biometrika **20**a:299 (Dec.) 1928. Pryor, H. B., and Stolz, H. R.: Determining Appropriate Weight for Body Build, J. Pediat. **3**:608 (Oct.) 1933.

5. Miles, W. R., and Root, H. F.: Weight and Physical Measurements After Thyroidectomy, Arch. Int. Med. **39**:605 (May) 1927.

Recording and Plotting.—For recording, a table is printed in the lower right quadrant of each sheet to receive twenty-four dated entries of the several measurements, preferably made within a fortnight of the birthday or of the half-year of age. When the table is filled, additional measurements can be recorded on the back.

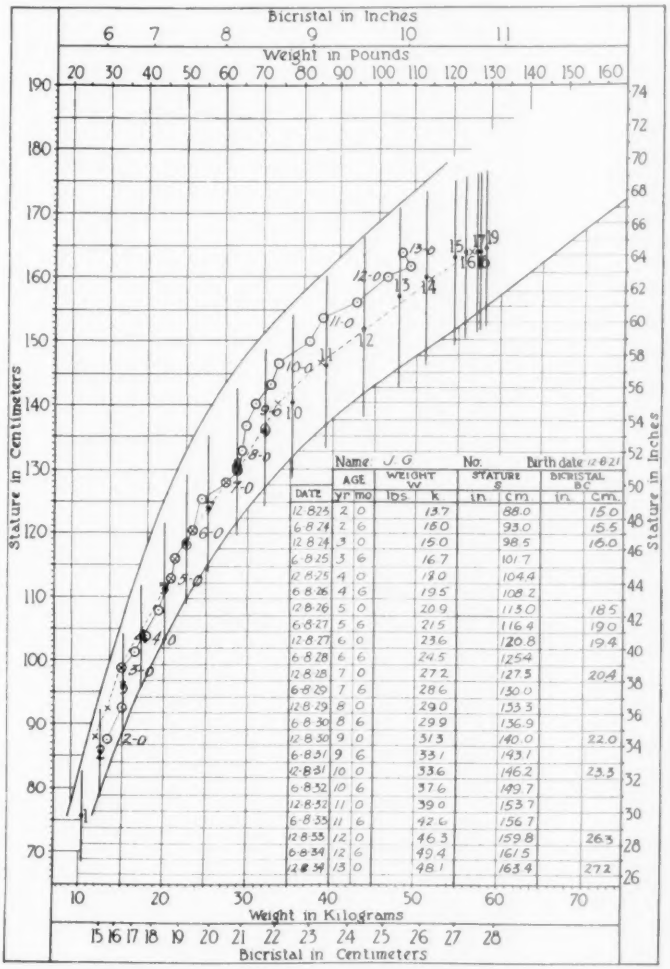

Chart 4.—Graph for a tall, slender girl. Every circle in the curve for height indicates moderate acceleration of growth. The weight until the age of 8 was that of the average girl; after that time the child was relatively a little thinner. At the earlier ages the crosses for bicristal diameter coincided remarkably with the circles for weight. One might hazard the prediction that the child will later tend to gain enough weight to bring the circles nearer the crosses again.

In plotting, each pair of values for stature and weight may be registered as a circle and each pair for stature and bicristal diameter as a

cross, with the age expressed in years and months beside them. Points may be located with the aid of a large celluloid triangle. The curve for stature and bicristal diameter when used can be further distinguished from the main curve for stature and weight by colored ink.

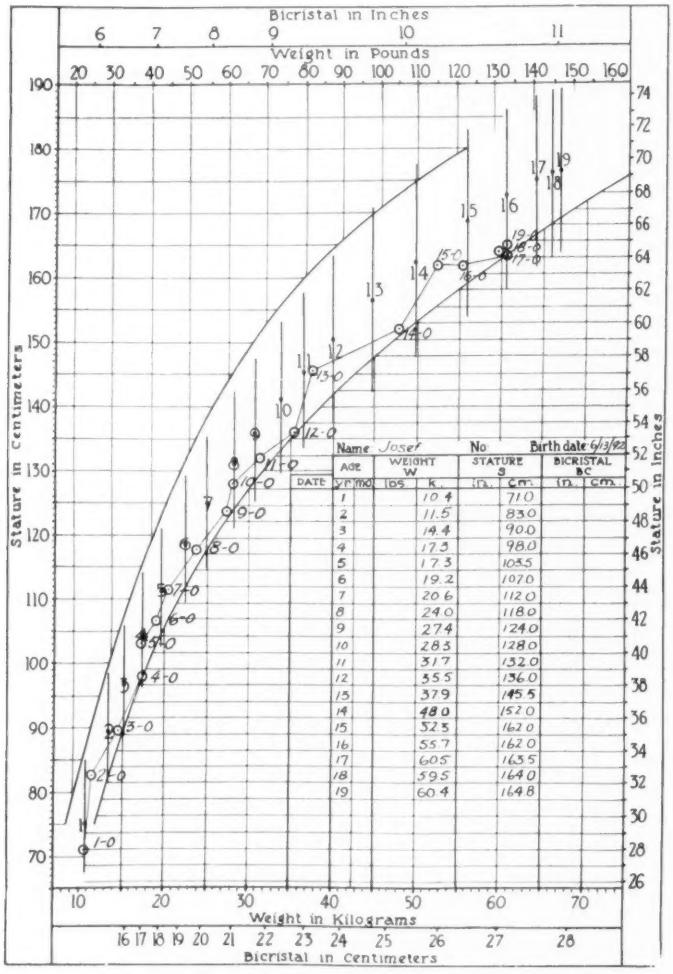

Chart 5.—Graph for a short, stout boy (Guttmann's subject Josef [Guttmann, M.: Einige Beispiele individueller körperlicher Entwicklung, Ztschr. f. Kinderh. **13**:248, 1915]). The stature was short throughout the period of observation. Between the ages of 6 and 12 the boy was shorter than 96 per cent of his age-mates; in adolescence the height increased to that of a small but normal adult. The weight was relatively high, the circles falling several times at the very limit of the stream. Unfortunately, there is no record of the bicristal diameter to give a hint of the size of the bony frame.

Sample Plots.—In charts 3, 4, 5 and 6 are shown plots for children of different types of build—three for normal children and one (chart 6) for a child with possible hyperthyroidism.

Mr. H. T. Castberg made the drawings.

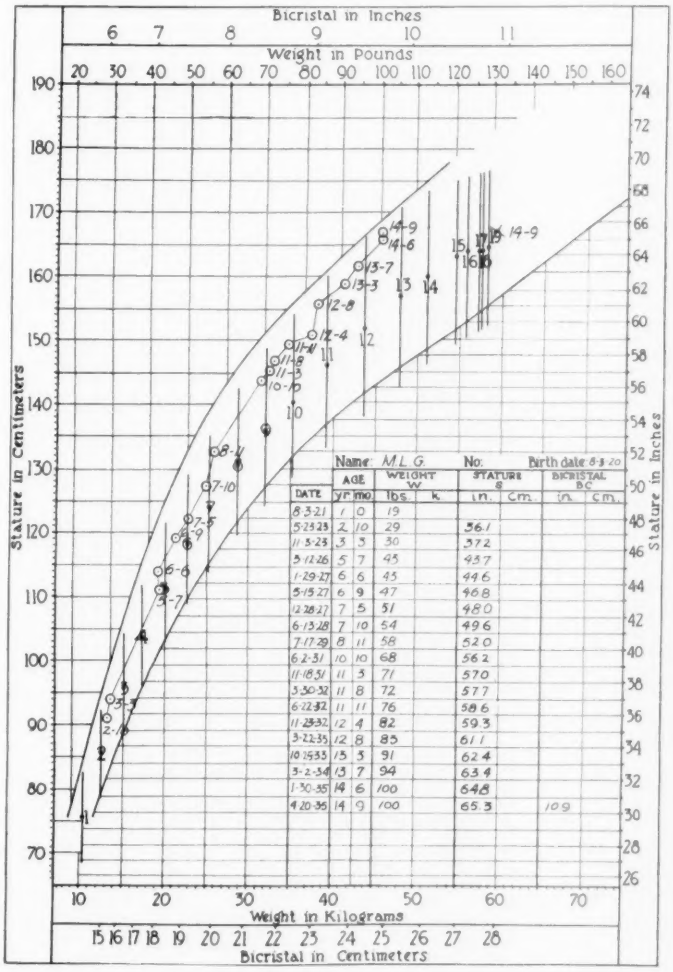

Chart 6.—Graph for a very thin girl. The stature was that of the average until the last two years, when it became moderately increased; the weight was low and showed a tendency to become progressively lower. Although the circles for weight and stature are within the open area, the child looked undernourished. The bicristal diameter at the last visit confirmed the clinical diagnosis in that the cross for the relation of bicristal diameter and stature fell well to the right of the stream at the same time that the circle for weight was far to the left.

THE PATHOLOGY OF STEATORRHEA

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Steatorrhea as a separate clinical entity seems not to be generally recognized. The term has been used in the description of several conditions having as a prominent symptom excessive amounts of fat in the feces. Under the heading "Steatorrhea" in the latest volumes of the "Quarterly Cumulative Index Medicus" the reader is referred to "Celiac Disease," under which he finds references to articles under a great variety of titles. Most of the terms used are recognized as synonyms for celiac disease, but under such titles as "Congenital Steatorrhea," "Congenital Pancreatic Steatorrhea with Infantilism" and "Pancreatic Steatorrhea in Children" a disease may be described which has a symptomatology and a clinical course quite different from celiac disease as generally pictured.

Perhaps congenital steatorrhea is the best term, since it implies one of the chief characteristics of the disease. The symptoms are uniform. There are frequent and rather voluminous stools from the first weeks of life, with failure to gain weight properly in spite of a sufficient intake of food, even when breast milk alone is fed. When the child is given artificial food the stools are very bulky, greasy and rancid and coated with droplets of free fat; from four to six or more stools of this type are passed daily. When butter, cod liver oil or similar distinctive fatty substances are fed, they are often passed from the bowel in an apparently unchanged state. With a diet low in fat, the stools more nearly approach a normal appearance. Poor nutrition, sometimes associated with delayed growth in stature, a protuberant abdomen and a stubborn persistence of digestive disturbances in spite of careful dietary management, characterizes the clinical course. A further characteristic is a lack of resistance to infection of the respiratory tract. Nearly all of the deaths reported were due to bronchopneumonia, and when necropsy was performed the lungs exhibited a distinctive pathologic condition.

Garrod[1] in 1913 made the first report of which I have been able to find a record. They reported the cases of two children in

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Read before the American Pediatric Society at Cleveland on May 2, 1935.

From the departments of pediatrics and pathology of the Presbyterian Hospital and of Rush Medical College of the University of Chicago.

1. Garrod, A. E.: Congenital Family Steatorrhea, Quart. J. Med. **6**:242, 1912-1913.

a family of five whose parents were first cousins and who since birth had passed from the bowel liquid fat which solidified on cooling. There were no signs of infantilism in these children, and both of them seemed to be otherwise in good health. One of these patients was studied.

In 1920 Miller and Perkins [2] remarked that only one case of congenital steatorrhea had been studied up to that time (Garrod's case). Acquired steatorrhea, they stated, is a well known symptom, and the most clearly defined cases are those in which it is associated with acquired disease of the pancreas.

Clarke and Hadfield [3] reported a case in 1924 with a typical clinical course, in which the child died at the age of 4½ years of bronchopneumonia. The necropsy in this case will be referred to later.

Two cases were reported by Harper [4] in 1930, one with necropsy. Both of the children died of bronchopneumonia at about 1 year of age.

Siwe [5] reported a case, together with the observations at necropsy, in 1932. Death occurred when the child was 2 years of age, from a respiratory infection.

Hess and Saphir,[6] in Jannary 1935, reported three cases with necropsy in each instance. I believe that in at least the first two of these cases, and probably in the third, the condition belonged in the group described by the term steatorrhea.

A study of the literature plainly shows the confusion regarding the clinical conditions classified as celiac disease. Certainly many conditions have been improperly so classified largely because of the lack of definite knowledge of pathology of the disease. Some conditions now being called celiac disease eventually may be separated from this general classification if there is sufficient evidence of a definite correlation between the clinical and the pathologic picture. It is with the hope of aiding in establishing such a correlation that the following two case reports are presented. Both patients were seen in private practice and were under constant observation from the time of their birth until their death; the first patient for fourteen and a half years and the second for four and a half years.

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2. Miller, R., and Perkins, H.: Congenital Steatorrhea, Quart. J. Med. **14**:1, 1920.

3. Clarke, Cecile, and Hadfield, Geoffrey: Congenital Pancreatic Disease with Infantilism, Quart. J. Med. **17**:358, 1923-1924.

4. Harper, Margaret H.: Two Cases of Congenital Pancreatic Steatorrhea with Infantilism, M. J. Australia **2**:663 (Nov. 15) 1930.

5. Siwe, S. A.: Total Agenesia of the Exocrine Portion of the Pancreas, Deutsches Arch. f. klin. Med. **173**:339 (July 25) 1932.

6. Hess, J. H., and Saphir, O.: Celiac Disease (Chronic Intestinal Indigestion): A Report of Three Cases with Autopsy Findings, J. Pediat. **6**:1 (Jan.) 1935.

REPORT OF CASES

CASE 1.—*History and Course.*—Barbara W., the first child of healthy parents, was born normally at term, weighing 6 pounds and 8 ounces (2,955 Gm.). Difficulties with feeding characterized the first fifteen months of her life; for three months she was given breast milk complemented by a simple modified milk formula, and after that, various modifications of milk, including albumin milk, evaporated milk and even breast milk. Cereals were added to her diet when she was 6 months old and vegetables and egg yolk when she was 8 months old. She was always hungry and took all that was offered her, but at 1 year of age she weighed only 14 pounds (6,364 Gm.). Aside from her failure to gain weight, the clinical course was characterized by frequent stools, always large and rancid and usually containing liquid fat or oil. Whenever cod liver oil was given or butter was part of her diet, the substance was passed in an apparently unchanged state. This condition characterized the stools throughout the fourteen years of her life.

She was kept on a diet relatively rich in protein and low in fat, and after she was 15 months old she gained weight fairly well; at 2 years of age she weighed 27.5 pounds (14.5 Kg.), and at 5 years she weighed 40 pounds (18.2 Kg.) and was 43 inches (109 cm.) tall. Her general health continued to be good; at 10 years her weight was 61¼ pounds (27.8 Kg.) and her height 52½ inches (133 cm.).

When she was 11 years old she acquired an infection of both maxillary sinuses and chronic bronchitis, from which she did not recover. In the last year of life she had an almost daily rise in temperature; she coughed up large quantities of purulent material and had a constant purulent nasal discharge. There was no improvement in spite of careful treatment. No evidence of tuberculosis was ever obtained. Mantoux tests and examinations of sputum gave negative results.

Examination of the urine at various times during her life and in the last months consistently gave negative results for sugar. Examination of the blood showed nothing in the last months except moderate secondary anemia and leukocytosis, with from 20,000 to 25,000 white cells per cubic millimeter and from 70 to 72 per cent polymorphonuclears.

From earliest infancy she had had a protuberant and flatulent abdomen. No appearance of infantilism characterized her development; her height and stature closely approximated the normal average for her age until she was 11, although her weight was usually considerably below the average. After the eleventh year growth was retarded, but the development of secondary sex characteristics was not. The essential findings during the last three years of her life were: bilateral purulent maxillary and ethmoid sinusitis and purulent bronchitis and bronchiolitis, associated with extreme emaciation in the later months.

Necropsy.—Macroscopic Examination: Both pleural cavities were free from adhesions and fluid. The lungs showed marked emphysema. The cut surface showed a large amount of purulent material exuding from the larger bronchi, and the smaller bronchioles were filled with the same material. Smears of material from the surface of the lung gave negative results for tubercle bacilli. The pancreas appeared normal, and the ducts were patent. There was evidence of recent fibrinous pericarditis. The valves of the heart were normal, but the myocardium was pale. Ascites was present, and the liver and spleen were enlarged and showed chronic passive congestion.

Microscopic Examination: The pancreas showed very marked alterations; only a few acini were found, and many of these were markedly dilated. The acini were separated by fibrous tissue, fat and granulation tissue of a subacute

type. In one main duct the lining was desquamated and the wall thickened by hyalinized fibrous tissue. There was an average of one island of Langerhans to every low power field. In sections of the lungs there were nodular regions, 2 or 3 mm. in diameter, the central portions of which were made up of desquamated cells surrounded by a dense layer of fibrous tissue composed of both the mature and the immature type and with giant cells in the tissue. Outside this layer there

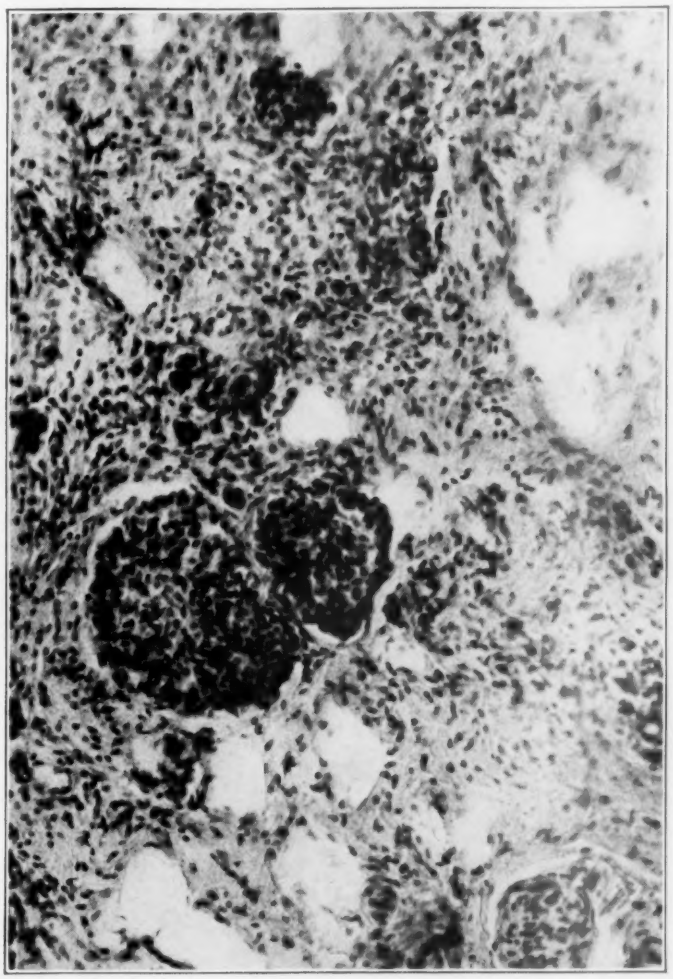

Fig. 1 (case 1).—Photomicrograph of the pancreas, showing atrophy of the acini, condensation of the stroma and relative decrease of the islands of Langerhans.

was a markedly vascular fibrous tissue with irregular infiltrations of lymphocytes and plasma cells. In another similar but smaller region there was a dilated small bronchiole the lumen of which was filled with polymorphonuclear leukocytes and desquamated epithelial cells, and surrounding it there was vascular granulation tissue with infiltrated plasma cells and lymphocytes. In another

region a large bronchiole was seen with the lumen occupied by a fairly solid mass of mucus in which were embedded polymorphonuclear leukocytes.

CASE 2.—*History and Course.*—Jane C., the first child of healthy parents, was born normally at term, weighing 5 pounds and 1¼ ounces (2,304 Gm.). She was a small infant but presented no physical or physiologic signs of prematurity.

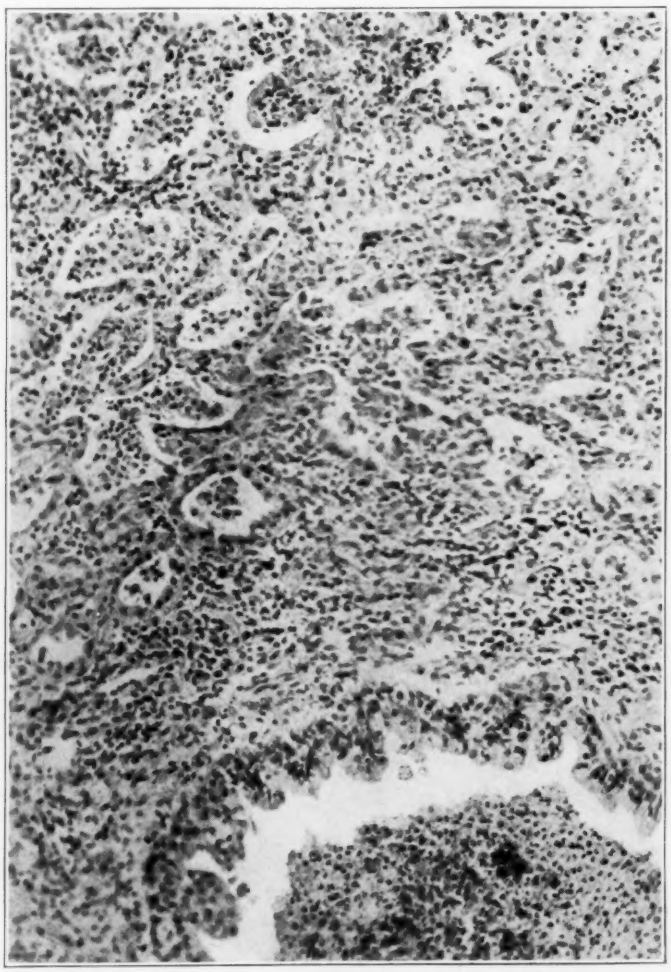

Fig. 2 (case 1).—Photomicrograph of a lung, showing acute bronchitis, atelectasis and acute bronchopneumonia. In addition to polymorphonuclear cells, the walls of the alveoli contain an increased number of histiocytes and fibrocytes.

In spite of getting sufficient breast milk she was barely ½ pound (227 Gm.) over her weight at birth at 7 weeks of age and had had from seven to eight large loose stools daily from the first week. On a diet of breast milk complemented with milk formulas high in protein and low in fat she made some improvement, but she gained slowly and the stools continued to be loose, bulky and rancid. At

4 months she was 3½ pounds (1,600 Gm.) over her weight at birth and had a protuberant abdomen. Breast feeding was discontinued, and various modifications of milk were given. She did best on fat-free powdered milk. Every attempt to add fat to her diet was followed by the appearance of neutral fat in the feces. Cod liver oil, when given, appeared in the feces apparently unchanged. At times the stools were firm, but they were always bulky, greasy and rancid as well as

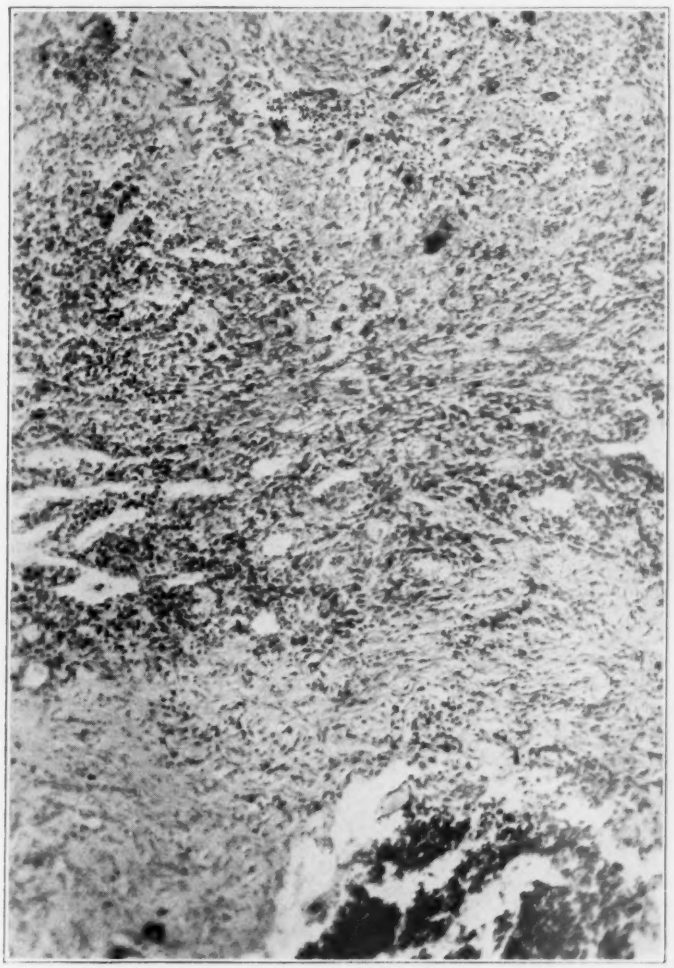

Fig. 3 (case 1).—Photomicrograph of a lung, showing a subpleural nodule consisting of chronic granulation tissue in which there are a few multinucleated giant cells of the Langerhans type.

frequent. At 1 year of age she was 8½ pounds (3,873 Gm.) over her weight at birth. At 4 years she weighed 27 pounds (12.25 Kg.) and was 35¾ inches (91 cm.) tall, which approximates the average for a child of 2 years. She continued to have the same type of stools that she had had during her earlier years in spite of a diet high in protein and low in fat.

Two months before her death, at the age of 4½ years, she contracted an infection of the respiratory tract. Bronchopneumonia and otitis media developed from this, and for the last seven weeks she had symptoms of bronchopneumonia, which showed no tendency to subside.

On several occasions during the last two weeks of her life sugar appeared in the urine.

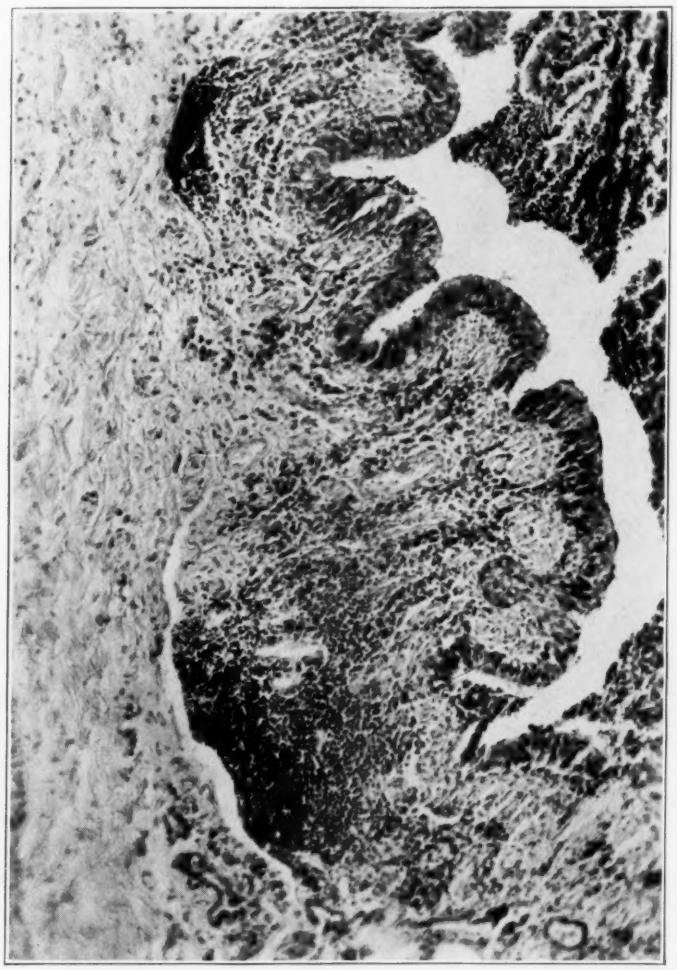

Fig. 4 (case 2).—Photomicrograph of a lung showing chronic bronchitis characterized by plasma cell and round cell infiltration of the submucosa, hyperplasia of the lymphoid tissue, increase of the collagenous fibrous tissue and acute bronchitis with occlusion of the lumen by polymorphonuclear leukocytes and fibrin.

Necropsy.—Macroscopic Examination: The lungs showed extensive subacute lobular pneumonia, miliary abscesses, marked mucopurulent bronchitis and bronchiolitis and acute suppurative lymphangitis. The pancreas was a hard mass of light gray glistening tissue with a few disseminated, irregular, light grayish-

yellow spots. There was no typical pancreatic tissue except at the head in a region about 6 cm. long, in which there were some small lobules. The pancreatic duct at the head of the pancreas was very narrow. The gallbladder was only 2 cm. long. The common and hepatic bile ducts were narrow.

Microscopic Examination: In sections of the firm nodules in the lung the alveolar walls were thick and the lumens small. In the alveolar walls were many

Fig. 5 (case 2).—Photomicrograph of the pancreas altered by atrophy of the acini, dilatation of a pancreatic duct and relative increase of the stroma. Two islands of Langerhans are present.

cells, chiefly epithelioid cells, polymorphonuclear leukocytes and a few fibroblasts. Within the alveoli there were erythrocytes, polymorphonuclear leukocytes and a pink-staining granular material. The lumens of the bronchioles were filled with an exudate of polymorphonuclear leukocytes, and in the surrounding tissue there was proliferation of the fixed tissue cells together with a slight infiltration of

polymorphonuclear leukocytes. There were also channels the lumens of which were filled with a similar exudate, with the surrounding tissue thickened by infiltration of polymorphonuclear leukocytes.

In sections of the tail of the pancreas there was an abundance of fibrous tissue, many blood vessels and nerves and scattered islands of epithelial tissue as large as the average glomerulus of a kidney. These were composed of cells with round or oval nuclei and an abundance of cytoplasm. They were buried in a moderately heavy fibrous network. In addition there were from eight to ten smaller collections of similar cells. There were marked fatty changes in the liver.

In a search through the literature I have been able to find four other cases in which the condition exhibited the clinical picture just described and in which necropsy was performed. In all of these the pathologic changes reported were practically identical with those in the two cases recorded here. At least two of the cases reported by Hess and Saphir [6] would seem to belong in this group clinically, and in them the pathologic changes were similar to those seen in my cases.

There have been several other cases classified under celiac disease, or a synonymous term, in which there were marked pathologic changes in the pancreas. They may have been cases of steatorrhea, but the clinical histories are either lacking or not sufficiently definite to warrant their inclusion (for example, the cases reported by Passini,[7] Schick and Wagner,[8] Mautner [9] and Gross [10]).

SUMMARY

Exhaustive treatises on celiac disease have appeared in recent years by Fanconi,[11] Lehndorf and Mautner [12] and Parsons.[13] These have added greatly to the knowledge of what Fanconi called the celiac syndrome. There is still, however, scant information concerning the pathology and no uniformity of opinion concerning the pathogenesis.

7. Passini, F.: Pankreaserkrankung als Ursache des Nichtgedeihens von Kindern, Deutsche med. Wchnschr. **45**:851, 1919.

8. Schick, B., and Wagner, R.: Ueber eine Verdauungsstörung jenseits des Säuglingsalters (Atrophia pluriglandularis digestiva), Ztschr. f. Kinderh. **35**:363, 1923.

9. Mautner, H.: Die Herter-Heubnersche Verdauungsinsuffizienz, Klin. Wchnschr. **4**:164, 1925.

10. Gross, F.: Pankreasatrophien im Säuglings- und Kindesalter, Jahrb. f. Kinderh. **112**:251, 1926.

11. Fanconi, G.: Der intestinale Infantilismus und ähnliche Formen der chronischen Verdauungsstörungen; Ihre Behandlung mit Früchten und Gemüsen, Berlin, S. Karger, 1928.

12. Lehndorf, H., and Mautner, H.: Die Coeliakie: Herters intestinaler Infantilismus, Heubners schwere Verdauungsinsuffizienz jenseits des Säuglingsalters, Ergebn. d. inn. Med. u. Kinderh. **31**:456, 1927.

13. Parsons, L. G.: Celiac Disease, Am. J. Dis. Child. **43**:1293 (May, pt. 2) 1932.

The term congenital steatorrhea has been used to describe a fairly definite clinical condition which differs from the usual picture of celiac disease in the following respects: 1. The onset is in the first weeks of life regardless of the type of feeding. 2. The stools contain an excessive amount of neutral fat as compared to the amounts of fatty acid and of soaps. 3. Free fat in the form of an oily substance often is passed with the feces in large amounts when such a food as butter, cream or cod liver oil is fed. 4. The patient never overcomes this digestive abnormality.

In the patients who have presented this clinical picture during life necropsy has revealed a constant pathologic process, i. e., marked fibrosis and great diminution in the amount of secretory gland tissue in the pancreas and bronchopneumonia in the lungs, usually of a subacute type with purulent bronchitis and bronchiolitis and sometimes with numerous widely disseminated miliary abscesses and changes in the alveolar walls indicative of chronic irritation.

The cause of the characteristic changes in the lungs is a subject deserving more study. The lack of fat-soluble vitamins or of some other factor, owing to the defective digestion of fats because of the poorly functioning pancreas, suggests itself as one explanation. Another possibility is that the lung tissue may be directly damaged by irritating substances, the products of abnormal digestion, carried to it in the venous blood.

Dr. Carl W. Apfelbach performed the necropsy reported in case 2 and made the microscopic examination of the organs in both cases.

DISCUSSION

Dr. Daniel C. Darrow, New Haven, Conn.: I have been much interested in the cases of steatorrhea in New Haven since I observed a case of the type which has been described in the paper just read. The patient was one of three in his family to have steatorrhea.

The differentiation of pancreatic insufficiency from celiac disease, which is the type of steatorrhea ordinarily seen, I think, has been studied most thoroughly by Thaysen. He pointed out in his articles on these syndromes that the important question in the examination of the stools is probably not how much neutral fat is present or whether the fats are split into fatty acids and soaps but whether there is evidence of deficiency in the absorption of nitrogen; in other words, patients with true pancreatic insufficiency with diminution in the amount of secretory gland tissue will show deficiency in the absorption of nitrogen. The other differential point is that a diabetic sugar tolerance curve occurs in some cases of pancreatic steatorrhea, while a flat sugar tolerance curve occurs in celiac disease.

Presumably the one patient of whom Dr. Parmelee spoke who had glycosuria would have shown a diabetic sugar tolerance curve. However, I do not think that the absence of a diabetic sugar tolerance curve excludes the possibility that the patient had pancreatic steatorrhea, but its occurrence indicates fibrosis involving the pancreatic islands as well as the acini.

When the pancreatic ducts of dogs are tied, flat sugar tolerance curves like those given by persons with celiac disease have been demonstrated.

The other point brought up by Dr. Parmelee is the interpretation of the pathologic condition of the lungs. The patient I observed showed clinical xerophthalmia. I feel that the evidence of sinusitis and bronchitis is probably dependent on the epithelial changes that accompany subclinical deficiency of vitamin A.

I have observed deficiency in vitamin A clinically in a patient who had defective absorption of fat owing to obstruction of the bile ducts. Similar observations have been made by Bloch. Consequently in a case of deficiency in the absorption of fat one must consider deficiency in the absorption of vitamin A.

Dr. Isaac A. Abt, Chicago: Did Dr. Parmelee note any osteoporosis in these cases?

Dr. Arthur H. Parmelee, Chicago: In answer to Dr. Darrow's question: In the pathologic picture of the pancreas there was a decrease in the number of islands of Langerhans. It is reasonable to expect there might have been glycosuria. However, glycosuria was not shown by either patient, except that one (case 1) did have sugar in the urine on several examinations during the last two weeks of life.

Xerophthalmia was not present at any time in either of the two cases reported here or in a third case which I think belongs to this group but in which necropsy was not permitted. The fact that xerophthalmia did not develop in either child, although one lived fourteen and one-half and the other four and one-half years, is, I think, an argument against the theory that a lack of fat-soluble vitamin satisfactorily accounts for the pathologic condition of the lungs.

I prefer to think of the type of pathologic process in the lungs as perhaps the result of the blood-filtering action of the lung; substances brought directly to the lungs in the venous blood may have some direct damaging or irritating effect on the tissue.

In reply to Dr. Abt's question regarding the osteoporosis so frequently observed in true celiac disease, I may say that it was not present in these cases. This is, I think, an argument in favor of steatorrhea's being a separate clinical disease and not the same as celiac disease. In neither case was spasmophilia present.

MALDEVELOPMENT AND MALDESCENT OF THE TESTES

II. FURTHER OBSERVATIONS ON TREATMENT WITH THE ANTERIOR PITUITARY-LIKE GONADOTROPIC HORMONE

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BROOKLYN

In a previous paper [1] I reported the results of treatment with anterior pituitary-like gonadotropic hormone from the urine of pregnant women in a series of fourteen boys who showed underdevelopment of the genital tract. The information which follows is based on a study of these fourteen patients. A brief review of the facts will be given and then I shall endeavor to report additional observations and deductions which I made during and after the administration of this anterior pituitary-like gonadotropic hormone from the urine of pregnant women.

Three of the patients (cases 10, 13 and 14) dropped out before treatment was completed. Two of these did not receive sufficient therapy to produce beneficial results. The third patient (case 14) received 36 cc. of the anterior pituitary growth hormone over a period of three months without the anterior pituitary-like gonadotropic hormone, but he showed no immediate response. Before treatment with the anterior pituitary-like gonadotropic hormone could be administered he dropped out. During the period he was out, no treatment was given; yet when he returned six months later, although the external genitals were still hypoplastic, the gonads showed a marked increase in size. It appears that this development can hardly be attributed to treatment with the anterior pituitary growth hormone, even though the preparation employed also contained gonadotropic and thyrotopic principles; this is considered, therefore, as one of the few instances of spontaneous development.

For the eleven other patients in this series, who did receive sufficient therapy, the duration of treatment with the anterior pituitary-like gonadotropic hormone varied with the type of genital underdevelopment.

From the Endocrine Clinics of the Department of Pediatrics, the New York University Medical College, the Children's Medical Service of the Third Medical Division, Bellevue Hospital, and the Beth-El Hospital.

Presented, in part, before the New York Endocrinological Society, Jan. 23, 1935. Presented at the Nineteenth Annual Convention of the Association for the Study of Internal Secretions at Atlantic City, June 11, 1935.

1. Dorff, G. B.: Maldevelopment and Maldescent of the Testes: Report of Treatment with the Anterior Pituitary-Like Gonadotropic Hormone from the Urine of Pregnant Women, Am. J. Dis. Child. **50**:649 (Sept.) 1935.

Those patients (cases 3, 5 and 11) showing descended but hypoplastic testes and hypoplastic external organs (a small penis and poorly formed scrotum) were generally treated for from five to ten months. As a result, all of them responded by definite increase in the size of the testes and by a subsequent increase in the size of the penis, with a well formed scrotum and development, in some, of pubic hair.

Those patients showing unilateral or bilateral cryptorchidism in addition to hypoplasia of both the gonads and the external genitals (eight cases) required longer periods of treatment, ranging from eight to thirteen months. Of this group, six patients at the end of treatment showed complete descent and normal development of the testes and external genitals. Of the other two, one patient (case 4), who originally showed an apparent absence of one testis and hypoplasia of the other, did not show complete descent and is therefore still under treatment, but the testis which originally was absent appeared and descended to a high scrotal position, the hypoplastic testis was tripled in size and the external genitals were markedly stimulated. In the second patient (case 2) who did not respond completely the penis, the homolateral lobe of the prostate, the epididymis and one testis responded markedly, but the other testis, originally absent, did not appear, and for this reason a mechanical obstruction or congenital absence is suspected.

Reactions to the anterior pituitary-like gonadotropic hormone, such as fever, retching, vomiting and lassitude, often followed when this product was used clinically. Today, however, with the purification of this hormone, such reactions to the usual dosage have been eliminated. As to the therapy, the usual dosage for hypoplasia, or hypoplasia and cryptorchidism, was 250 rat units of the hormone[1a] per injection given from three to five times per week; however, when the gonadal response was slow (as indicated by enlargement of the testes and particularly by congestion of the external genitals) the doses were then increased to from 500 to 1,000 rat units and were given daily until the required reaction was obtained. No marked ill effects were noted from doses of 1,000 rat units given over a number of successive injections. There was no doubt that response in some of these patients was more marked than in others, particularly on the penis. This was true even when the patient was given the usual dosage; in other words, there were individual responses to the dosage, some responding to the same dosage better than others. The largest aggregate dose in rat units given to cause complete development was given in case 8, 46,266 rat units administered over a period of thirteen months.

1a. E. R. Squibb & Sons supplied the anterior pituitary-like gonadotropic hormone (follutein) and the anterior pituitary growth hormone (now available as anterior pituitary extract-Squibb).

With such chronic treatment the question arises whether any antihormonal action to the anterior pituitary-like hormone was observed. It did appear even in this limited study that certain of the patients required increased doses, or more frequent injections, as treatment progressed, and when these were given the congestive response of the external genitals was much better. Yet there were several patients who responded to the usual dosage and required no unusual increase in dosage or frequency in treatment. Whether, therefore, this was due to the production of antihormones, as Collip [2] believed, or to the stimulating capacity or potency of the dose administered and the responsive capacity of the receptor tissues or organs, as Smith [3] has suggested, is not clear. For example, one patient (case 8) seemed slower in his response to treatment with the anterior pituitary-like gonadotropic hormone than was usual. He received about ten daily injections of increased dosage without showing any congestion of the external genitals; yet eventually he responded and a completely satisfactory result was obtained without increased dosage. Another patient (case 2), after treatment was discontinued because of an apparent enlargement of the prostate gland, showed the same congestive reaction in the genital tract to the usual dosage on the resumption of treatment three months later, and afterward this same patient, when the dosage was increased to 500 and 1,000 rat units per injection for a number of injections, showed a more acute congestive response of the external genitals and further development of these and the gonads. However, in no case was there regression of genital development at any time while treatment was being administered.

While all the patients in this series had the so-called adiposogenital type of dystrophy, i. e., obesity plus genital hypoplasia, there were other differences in their make-up which warranted a classification of these patients into two distinct types. This classification was based on whatever gland I believed was primarily responsible for the genital hypoplasia, as follows: [4]

1. Those with hypothyroidism, who always showed evidence of definite delay in osseous development and often, but not necessarily, a history of or the presence of somatic retardation, in addition to genital

2. Collip, J. B.: Some Recent Advances in the Physiology of the Anterior Pituitary, J. Mt. Sinai Hosp. **1**:28 (May-June) 1934.

3. Smith, P. E.: General Physiology of the Anterior Hypophysis, J. A. M. A. **104**:548 (Feb. 16) 1935.

4. A classification of the types of adiposogenital dystrophy is suggested for use in the clinic, namely, AGD-hypothyroid, AGD-hypogonad, AGD-hypopituitary, AGD-Fröhlich, etc. The term affixed to AGD indicates what I believe to be the primary offending gland for the genital underdevelopment. These types will be more fully discussed in a subsequent paper.

underdevelopment and obesity. The offending gland was considered to be the thyroid.

2. Those with hypogonadism, who almost always showed overgrowth and eunuchoidism, though with normal osseous development, in addition to sexual underdevelopment and obesity. The offending glands were considered to be primarily the gonads.

The patients with hypogonadism received no therapy prior to this study.

Several of the patients with hypothyroidism (cases 1, 2, 3 and 6) had received thyroid therapy prior to this study and had shown definite developmental progress, both mentally and physically, as a result of this therapy. This progress was reported in detail in a previous article.[5] In spite of these developments, in order that the effects of the anterior pituitary-like hormone could be evaluated, the thyroid therapy was discontinued, and only anterior pituitary-like hormone was given when this present study was instituted.

Since there were two groups of patients who had in common similar defects, namely, genital underdevelopment and obesity and characteristic dissimilar disturbances, for instance, osseous retardation and somatic defects in the patients with hypothyroidism, I shall endeavor to report on the efficaciousness of the anterior pituitary-like gonadotropic hormone in its correction of those disturbances common in both conditions and its correction of those disturbances characteristic only of one. Also, I shall attempt whenever possible to show the effectiveness of therapy with the anterior pituitary-like hormone as compared with the effectiveness of therapy with thyroid on those patients who received thyroid before the anterior pituitary-like gonadotropic hormone.

EFFECT OF THE HORMONE

Genital Development.—As has been stated already, when treated with the anterior pituitary-like hormone, the genitals of both types of patients responded definitely though in a varying degree, depending on personal differences and the variations in dosage as mentioned earlier in this paper. The first evidence of such stimulation resulting from the usual dosage was seen in the testes, which responded with enlargement and gradual descent. This was the case in those testes which were bilaterally hypoplastic and undescended. When there was unilateral cryptorchidism and hypoplasia of the other testis, the reaction of the external genitals, such as congestion of the penis and the scrotum and the unfolding of the scrotum, followed the apparent enlargement of the hypoplastic testis, even though the undescended testis had not as yet changed. When

5. Dorff, G. B.: Masked Hypothyroidism in Children: Osseous Development as an Aid in the Diagnosis, J. Pediat. **6**:788 (June) 1935.

both testes were in the scrotum but were hypoplastic, enlargement of these preceded the enlargement of the external genitals. The testes increased, in some cases to several times their original size, and even in cases in which they could not be definitely defined at first, the development in their size could be traced after a while, beginning with an indefinite mushy mass, then soon becoming more globular and finally taking on the form of a definite testis, which then began to enlarge and descend. This, I was inclined to believe, was the actual *modus operandi* in the development of an apparently absent testis in several of the cases, being more than the extrusion of a preformed testis from the abdomen into the canal, although the manner of descent into the canal was the same in both instances.

Of importance was the fact that the size of the testes could be increased by treatment with the anterior pituitary-like hormone only up to the physiologic limits for the age of the child and that subsequently, no matter how many more injections of the hormone were given (within the limit of time of the study), the testes did not appear to increase any further in size, although the external genitals gave a marked response. One patient in the series (case 5), with delayed sexual development, responded to treatment so markedly that the testes, which originally were the size of shelled hazelnuts, were tripled in size in a period of eight months of treatment with the anterior pituitary-like hormone (21,375 rat units). When he was seen six months after cessation of treatment with the hormone at the age of 13½, the testes had increased to the size of walnuts. The response of the testes of this patient, as compared with the response of those of some of the other patients, pointed to the fact that the response to the anterior pituitary-like hormone becomes more marked the closer the patient approaches puberty.

After this enlargement and descent, the next development occurred in the external genitals and sex accessories. That this development of the sex accessories should have been subsequent to the testicular stimulation indicates that there was production of the male sex hormone by the testes. After sufficient stimulation and development of the testes and consequent production of the sex hormone, the penis was markedly thickened and enlarged; the epididymis developed, and the scrotum filled out. Pubic hairs appeared and in one patient seminal emissions occurred (case 11). During the time of this development, when there was congestion of the external genitals in the course of treatment with the anterior pituitary-like hormone, especially when this reaction was at its height, frequent erection of the penis was noted in most cases.

All of the responses listed could be produced even in children too young for this development. Such development obviously is not desirable and should not be attempted before the advantages and dis-

advantages of such overstimulation have been carefully considered. In case 4, such overdevelopment of the external genitals and secondary characteristics occurred, and it was permitted in spite of the youth of the patient, since it was necessary to prolong the treatment in order to cause complete descent of one of the testes.

In all cases, with one exception, the prostate could not be defined after treatment. In the one exception, case 2, after 141 injections of 45,200 rat units given to cause a descent of an apparently absent left testis and to enlarge a small right testis, there was a tripling in size of the right testis with a prominence of the right lobe of the prostate but no response in the left testis or the left lobe of the prostate.

This series of patients showed no marked hernia accompanying cryptorchidism before treatment with the anterior pituitary-like hormone. Dilated inguinal rings, though, were noted in several prior to treatment. In some cases occasional pain was felt in the groin during the course of the treatment with anterior pituitary-like hormone. One patient (case 4), who originally had an apparently absent right testis and subsequently after some treatment presented a formed testis high in the right inguinal canal, also showed a markedly thickened rounded band the size of a lead-pencil extending upward from its upper pole. Later, with further treatment, the testis enlarged and descended to a high scrotal position, and at the same time the thickening receded to the size of the lead of a pencil. This, therefore, might have been a hydrocele or a ligamentum vaginale representing the rudimentary processus vaginalis. At no time was hernia produced as a consequence of the treatment.

On comparing the effectiveness of treatment with the anterior pituitary-like hormone with that of treatment with thyroid, it could be said that the response of the genitalia of the patients with so-called hypothyroidism was much greater and more marked after administration of the anterior pituitary-like hormone than after the administration of thyroid. This does not mean that previous therapy with thyroid was inefficacious, for it was noted that all the patients with hypothyroidism who originally showed absence of one or both testes subsequently presented testes in response to this thyroid therapy, though the testes were very small. The appearance of such testes under thyroid therapy was well in keeping with the opinion of Engelbach,[6] who felt that this form of genital underdevelopment was of the nature of congenital hypothyroidism. The greater response of the genitals to the anterior pituitary-like hormone was believed to be due to direct stimulation of the gonads and consequently to greater stimulation of the external genitals.

6. Engelbach, W.: Endocrine Medicine, Springfield, Ill., Charles C. Thomas, Publisher, 1932, vol. 2, p. 148.

Osseous Development.—As has been stated before, osseous retardation was characteristic of the patients with hypothyroidism. From observations made prior to the present study with the anterior pituitary-like gonadotropic hormone, I noted and reported that thyroid therapy, given to such patients over a reasonable period of time, produced a definite advance in ossification exceeding the normal advance for the same period and thus causing a decrease in the lag [5] in osseous development.

It can now be reported that in those patients who had received previous thyroid medication the anterior pituitary-like hormone caused a progression of osseous development, but this advancement was not as marked as when the patient was on the thyroid medication; i. e., the lag after treatment with the anterior pituitary-like hormone as compared with the lag after treatment with thyroid showed an increase, but the increase was not as great as it might have been had no therapy of any kind been given.

In addition, it can be stated that when the anterior pituitary-like hormone was given to a patient with hypothyroidism without previous thyroid therapy, it caused some progression in osseous development and thereby decreased slightly such lag, but the decrease in the lag was not as great as that in the patients to whom thyroid therapy was given prior to treatment with the anterior pituitary-like hormone. Generally, however, the anterior pituitary-like hormone produced only normal advancement of the bone for the period but did not overcome or decrease the previous existing lag. There were two exceptions, cases *2* and *7*, in which the lag decreased on treatment with the anterior pituitary-like hormone and there was an advance almost to normal osseous development.

In the patients whose osseous development was normal before treatment, as in the patients with so-called primary hypogonadism, the study showed that therapy with the anterior pituitary-like hormone produced no marked deviation from the normal osseous advance and that osseous development progressed as usual.

As to the reason for the advancement of osseous development in a patient with hypothyroidism treated with the anterior pituitary-like hormone, this advancement can be attributed to the direct stimulation of the anterior pituitary-like hormone on the gonads and perhaps not to an intermediary stimulation of the thyroid gland as might be expected. For it is known that in patients in whom an intense gonadal activity is present, as in the case of precocity due to adrenal, pineal or gonadal tumor, a rapid progression of osseous unfolding and a hastening of epiphyseal closure occur. It may here account for the advance in osseous development with the anterior pituitary-like hormone in the patients with hypothyroidism. Generally speaking, I do not think that

Observations on Fourteen Boys Treated with the Anterior Pituitary-Like Gonadotropic Hormone for Maldevelopment and Maldescent of the Testes *

Patient, Age in Years	Type and Appearance†	Genital Development Prior to Treatment	Therapy‡	Response of Genitals to Each Corresponding Treatment	Increment in Height, Inches: Period Prior to Treatment	Increment in Height, Inches: Period of Treatment	Calculated Optimum Increment in Height (Inches), Period of Treatment	Basal Metabolic Rate, per Cent: Before Treatment with A.P.H.	Basal Metabolic Rate, per Cent: During Treatment with A.P.H.	Basal Metabolic Rate, per Cent: After Treatment with A.P.H.	Osseous Development: Before Thyroid Therapy	Osseous Development: After Thyroid Therapy; Before Treatment with A.P.H.	Osseous Development: After Therapy; Treatment with A.P.H.
1 J. S. 8 ¾	Hypothyroid; eunuchoid; normal height	Testes not felt	1. Thyroid for 1 year 2. A.P.H. (36,665 rat units); 116 injections in 10 mo.	1. Pea-sized testes, high up in inguinal canal; no pubic hair 2. Testes tripled, in scrotum; good crop of pubic hair	2 in 8 mo.	1. 2 in 1 yr. 2. 2.75 in 10 mo.	2.1 1.66	—14.0‖	—9.0 —19.8	—16.6 —17.9 —11.2 —26.8 (Treatment resumed)	Retarded 20 mo.	Retarded 15 mo.	Retarded 20 mo.
2 A. B. 10	Hypothyroid; normal proportions; accelerated height	Pea-sized right testis in midscrotum; left testis absent; penis small	1. Thyroid for 1½ years 2. A.P.H. (45,200 rat units); 141 injections in 10 mo.	1. Right testis increased, in scrotum; left absent 2. Right testis tripled; penis markedly enlarged; good crop of pubic hair; right lobe of prostate defined	1.75 in 12 mo.	1. 3.5 in 18 mo. 2. 3.5 in 10 mo.	3.0 1.53	—23.5‖	—17.1 —11.2 (Treatment resumed) —21.5 — 8.3 — 5.4	—25.6 —23.0 —23.6	Retarded; poor massing	Slightly retarded	General advance; still poor massing
3 M. L. 8½	Hypothyroid; eunuchoid; normal height	Pea-sized testes in scrotum; penis of medium size	1. Thyroid for 7 weeks 2. A.P.H. (39,250 rat units); 135 injections in 10 mo.	1. No change 2. Testes tripled; penis enlarged; good crop of pubic hair	1.5 in 10 mo.	3.5 in 10 mo.	1.66	—18.0‖	—12.2	.....	.....	Retarded from 6 to 9 mo.	Some advance; retarded 6 mo.
4 P. L. 7¼	Hypothyroid; eunuchoid; normal height	Pea-sized left testis in scrotum; right testis not felt; penis small	A.P.H. (33,000 rat units); 114 injections in 13 mo.	Left testis tripled; right good sized high in scrotum; penis markedly enlarged; good crop of pubic hair	..	3.5 in 13 mo.	2.16	Uncooperative	+ 8.0	.....	.....	Retarded 12 mo.	Retarded 12 mo.
5 M. C. 12¼	Hypothyroid; eunuchoid; repressed height	Hypoplastic testes in scrotum; tending to retract; penis small, buried in mons	A.P.H. (21,375 rat units); 78 injections in 8 mo.	Walnut-sized testes in scrotum; penis increased; good crop of pubic hair	1 in 12 mo.	1 in 8 mo.§	1.20	.....	— 8.5	—14.4 — 2.4	.....	Retarded 24 mo.; poor bone structure	Retarded 24 mo.; better bone structure
6 J. H. 8	Hypothyroid; normal proportions; accelerated height	Small testes in canal; penis small	1. Thyroid for 18 mo. 2. A.P.G., 64 cc.; A.P.H. (5,312 rat units); 64 injections in 7 mo. 3. A.P.H. (16,204 rat units); 57 injections in 4 mo.	1. Slight descent of testes; slight increase in size 2. No apparent change 3. Testes tripled in scrotum; penis increased; no pubic hair	1 in 6 mo.	1. 3.5 in 18 mo. 2-3. 3.25 in 11 mo.	3.0 1.83	—15.8‖	—15.8	—18.6 —28.0 —28.6	Retarded 24 mo.	Retarded 16 mo.	Retarded 19 mo.
7 D. K. 8½	Hypothyroid; normal proportions; accelerated height	Small left testis in midscrotum; right testis not felt	1. A.P.G., 22 cc.; 22 injections in 2 mo. 2. A.P.H. (15,650 rat units); 72 injections in 7 mo.	1. Left testis, no change; right not felt; very small right testis felt high in canal 2 mo. after cessation of A.P.G.; no change in left testis 2. Left tripled in size, in scrotum; right testis increased in size in midscrotum	2.5 in 9 mo.	2.5 in 11 mo.	1.83	— 3.3	—17.3	.....	.....	Retarded 10 mo.	Almost normal

* All anthropometric readings are taken from Engelbach, W.: Endocrine Medicine, Springfield, Ill., Charles C. Thomas, Publisher, 1932, vol. 1. The age of the patient at the time of the institution of treatment with A.P.H. is given. For additional data on the patients of this series see footnote in the text.

† All the patients in this series had adiposogenital dystrophy (adiposity plus genital hypoplasia).

‡ Treatment with A.P.H. (anterior pituitary-like gonadotropic hormone) started in November 1933. A.P.G. indicates anterior pituitary growth hormone.

§ This patient gained 1 inch in height in the four months following cessation of treatment with A.P.H.

‖ Basal metabolic rates were taken before thyroid therapy.

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8 M. W. 10¼	Hypothyroid; eunuchoid; accelerated height	Left testis size of a large pea; pea-sized right testis, retracted; penis small, buried in mons	1. A.P.G., 63 cc.; A.P.H. (3,400 rat units); 63 injections in 5 mo. 2. A.P.H. (42,866 rat units); 150 injections in 8 mo.	1. No apparent change 2. Both testes tripled in scrotum; penis enlarged; good crop of pubic hair	..	3.25 in 13 mo.	2.17	—11.6	—11.6 —14.6 —15.7	—21.0 —13.1 —15.0	.....	Retarded from 18 to 24 mo.	Retarded from 12 to 18 mo.
9 M. S. 11¼	Hypogonad; eunuchoid; accelerated height	Marble-sized testes in canal; penis small, buried in mons; no pubic hair	A.P.H. (22,000 rat units); 80 injections in 7 mo.	1. Testes enlarged, high in scrotum; penis larger; many black pubic hairs	1.25 in 6 mo.	0.75 in 3 mo.	0.47	— 3.0	.....	.....	.....	Normal	.....
10 N. R. 11	Hypogonad; normal proportions; normal height	Pea-sized testes; penis buried in mons; no pubic hair	1. Observation for 20 mo. 2. A.P.G., 38 cc.; A.P.H. (3,916 rat units); 38 injections in 3 mo. discontinued	1. Testes slightly increased to size of small almond 2. Small testes, in scrotum, not much increase; few blond short pubic hairs	1.25 in 12 mo.	0.5 in 3 mo.	0.47	+ 8.0	.....	.....	.....	Normal	.....
11 L. W. 13½	Hypogonad; eunuchoid; accelerated height	Small testes in midscrotum; penis small; no pubic hair	A.P.H. (18,000 rat units); 75 injections in 5 mo.	Testes increased, in scrotum; penis enlarged; pubic hair present	1.5 in 6 mo.	1.5 in 5 mo.	0.75	—18.0	.....	.....	.....	Normal	.....
12 H. L. 6	Hypogonad; eunuchoid; normal height	Pea-sized left testis in midscrotum; right testis slightly larger in canal; penis small	1. Thyroid for 3 wk. 6 mo. prior to A.P.H. 2. A.P.G., 84 cc.; A.P.H. (10,000 rat units); 84 injections in 7 mo. 3. A.P.H. (15,000 rat units); 66 injections in 4 mo.	1. No change 2. Right testis slightly increased 3. Testes tripled, in scrotum	2 in 12 mo.	2 in 11 mo.	2.02	Uncooperative	.....	.....	.....	Normal	Normal
13 L. S. 9½	Hypogonad; eunuchoid; accelerated height	Small testes in scrotum; no pubic hair	1. Observation for 7 mo. 2. A.P.G., 8 cc.; A.P.H. (665 rat units); 8 injections in 1 mo.; discontinued	1. Small testes, the size of kidney beans, in scrotum; no pubic hair 2. No change 3. Examined 16 mos. later; no change	1 in 7 mos.	.. 1 mo.	0.17	— 9.3	.....	.....	.....	Normal	.....
14 D. G. 11¾	Hypogonad; eunuchoid; normal height	Almond-sized testes in scrotum; penis small; no pubic hair	1. Observation for 7 mo. 2. A.P.G., 36 cc.; 36 injections in 3 mo.; discontinued	1. Testes the size of almonds; penis small 2. No change (Examined 6 mos. later and showed two testes the size of large olives in the scrotum; the penis small and buried in mons; several white pubic hairs; gain of 2¼ inches in height since institution of treatment)	0.25 in 7 mo.	.. 3 mo.	0.47	—22.0	.....	.....	.....	Normal	.....

the anterior pituitary-like hormone could stimulate normal gonads sufficiently to accelerate an existing osseous retardation to such an extent that it would bring the osseous delay up to normal, for a patient with hypothyroidism requires thyroid medication to cause sufficient acceleration of the osseous development and in addition requires the anterior pituitary-like hormone if rapid development of the gonads is desired. Therefore, if complete genital and osseous development is desired, it is advisable to give therapy with both the anterior pituitary-like hormone and thyroid substance.

Height.—The height of the patient with primary hypogonadism in all cases (see table) exceeded the maximum height for the average normal boy of the same age. Under treatment with the anterior pituitary-like hormone the increment in height then became even greater than the increment for a similar period prior to any therapy.

In the patients with hypothyroidism to whom treatment with thyroid was given for a reasonable period of time prior to that with the anterior pituitary-like hormone, the increment in height with the thyroid medication was greater than that prior to a similar period of no therapy (case 1 excepted); also the increment was even greater than the calculated normal optimum increment in height for the period. Then, with the administration of the anterior pituitary-like hormone in the same patients with hypothyroidism who had received thyroid, the increment in height was still greater than, or at least equal to, that under thyroid therapy.

With the administration of the anterior pituitary-like hormone to those patients with hypothyroidism who received no prior therapy, the increment in height was generally greater than the increase in height for a similar period of no therapy.

With height as with osseous development, it may be said that while active gonads generally act as a check on height by stimulating a rapid progression of osseous development and by hastening epiphyseal closure, one need not go very far to see that when there is overactivity of the gonads, as in precocity (or at puberty), there is a spurt in height, although eventually the final height may still be below the normal.

Basal Metabolism.—Both groups of patients in this series, with one exception, prior to treatment had basal metabolic rates on the minus side, ranging from —3 to —23.5 per cent.

Unfortunately, I was unable to follow up the change in the basal metabolic rates in the patients with hypogonadism during and after treatment with the anterior pituitary-like hormone and therefore cannot report at this time on the metabolic rates of this group.

I was, however, able to check on the basal metabolic rates of the patients with hypothyroidism. An increase, though not too marked, was

noted in the metabolic rate of several patients during treatment with the anterior pituitary-like hormone, and after treatment the rates were lowered. Whether the thyroid gland was stimulated by the anterior pituitary-like hormone is not certain from these observations.

That the thyroid gland is not stimulated by injections of the anterior pituitary-like hormone had been shown previously by the experimental histologic studies of Hertz and Kranes [7] and of Collip and his associates [8] on male animals. It is also the opinion of Gaebler [9] that the urine of pregnant women administered in large single doses to dogs has no thyrotropic action, as evidenced by the lack of a prolonged rise in the basal metabolic rates in the test dogs. However, one of the four test dogs did show some sustained rise in the basal metabolic rate.

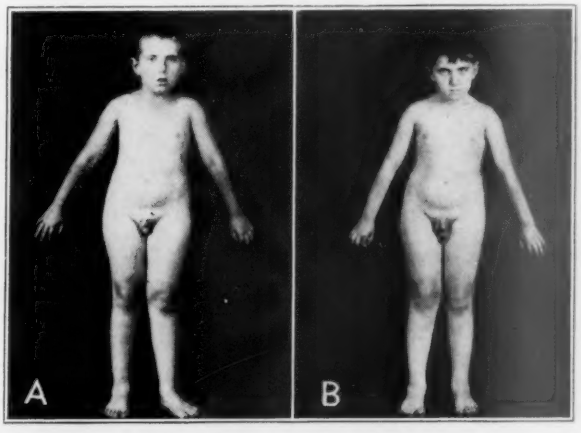

Fig. 1 (case 4).—*A* shows P. L. in July 1933, before treatment. *B* shows the patient in December 1934 after treatment with anterior pituitary-like gonadotropic hormone (33,000 rat units in thirteen months); the right testis, originally absent, can now be seen in the scrotum; the penis and the scrotum are markedly enlarged, and there is a generous crop of pubic hair, which is not visible in the photograph.

Weight and Body Contour.—Patients in this series were obese or overweight from the start. Under treatment with the anterior pituitary-like hormone there was an increase in weight in all cases even greater than that for such patients before treatment and certainly greater than the calculated optimum increment for a similar period in normal patients.

7. Hertz, S., and Kranes, A.: Exhaustion Phenomenon in Thyroid Produced by Pituitary Treatment: Histological Study of Rabbit's Thyroid Under Varying Degrees of Anterior Pituitary Therapy, Endocrinology **18**:415 (May-June) 1934.

8. Collip, J. B.; Selye, H.; Thomson, D. L., and Williamson, J. E.: Effect of Prolonged Administration of the Anterior Pituitary-Like Hormone on Pituitary and Thyroid, Proc. Soc. Exper. Biol. & Med. **30**:590 (Feb.) 1933.

9. Gaebler, O. H.: Action of the Anterior Pituitary-Like Substance of Urine on the Metabolism of Dogs, Endocrinology **19**:63 (Jan.-Feb.) 1935.

The persistence of obesity after complete correction of the underdeveloped genitals makes the relationship of obesity to the gonads questionable and brings up the possibility that such obesity might be due to the lowered basal metabolic rate or might be constitutional. Means for combating the obesity should be attempted through dietary restriction and whenever necessary with thyroid medication. In the present series, such means were not employed since this would have complicated the study of the effects of the anterior pituitary-like hormone.

The body contour of these patients was the so-called girdle type of obesity, showing mammary enlargement, trochanteric and abdominal pads of fat and in some instances genu valgum. Under treatment with the anterior pituitary-like hormone the genu valgum was improved in a number of cases. The obesity, however, persisted, although in general

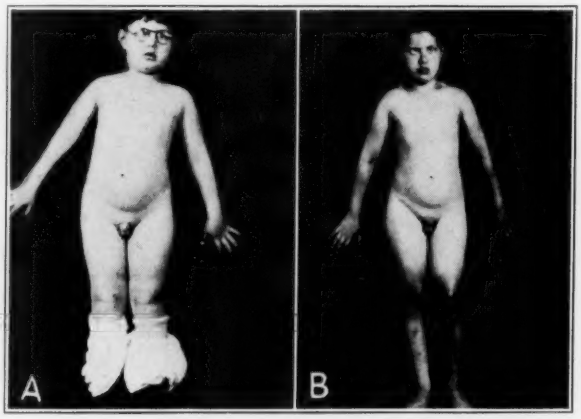

Fig. 2 (case 6).—*A* shows J. H. in November 1931, at the age of 6 years, before treatment with thyroid extract; there were two small testes in the canal. *B* shows the patient in July 1934, at the age of 8½ years, after seven months' treatment with 14,566 rat units of the anterior pituitary-like gonadotropic hormone. Note the enlarged testes in the scrotum and the change in body contour.

it appeared that there was a slight redistribution of the fat pads, especially in those patients who had received previous thyroid therapy.

The breasts showed no increased enlargement under this treatment; neither was there any complaint of pain in the mammary glands. With the exception of one patient, not in this series, no nodulations were present as a result of the treatment. This one patient, aged 9 years, complained of some pain in the left breast after having received about 17,000 rat units in 80 injections. On examination a tender tumefaction was felt around the nipple. With cold applications this tumefaction receded, and its presence was considered to be coincidental.

The facies took on the appearance of alertness and brightness, especially in those patients who received thyroid medication prior to treatment with the anterior pituitary-like hormone.

Hirsuties of the face or of the body, except in the pubic region, was not present.

Urinary Symptoms.—There was no evidence of increased frequency of urination or dysuria in any of the patients. One patient in the series (case 5), however, presented mild meatitis, but this cleared up in a few days. Several showed faint traces of albumin before or during treatment but no gross evidences of renal damage.

PSYCHIC EFFECTS

The psychic effects on these boys were significant, since prior to treatment they were aware of their genital inferiority and therefore were generally reticent and shy and shunned exposure of their genital

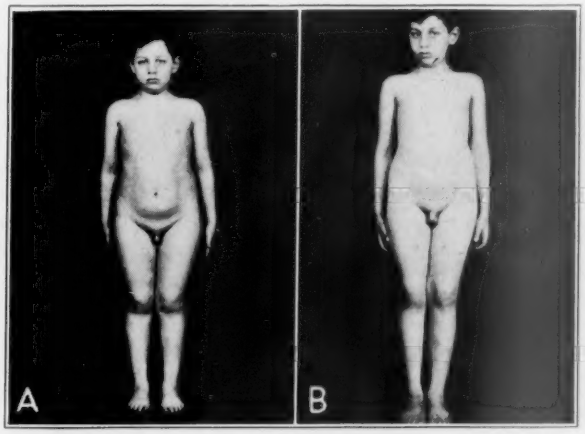

Fig. 3 (case 7).—*A* shows D. K. in March 1933, at the age of 8 years, before treatment; the right testis was not felt and the left testis was small in the midscrotum. *B* shows the patient in November 1934, after treatment with anterior pituitary-like gonadotropic hormone (15,650 rat units in one year); note the enlarged penis and the well formed scrotum; the left testis is tripled in size and the right testis is of medium size and in the midscrotum.

parts. With progression of treatment, effectual results were noted and consequently the boys gained assurance and initiative and tended to become more extravert. One patient (case 4), aged 9 years, who originally was somewhat backward mentally, with treatment showed marked improvement in this respect and developed to the point where he favored companionship. Later he even exposed his now developed genitals to his female playmates; however, this practice was stopped after he was chastised by his parents.

There was a change in the attitude of the parents with the development of the child, and this consequently was transferred and reflected in the mental set-up and attitude of the child.

SPONTANEOUS DESCENT AND ATROPHY OF THE TESTES

While it is true that some testes will descend and correct themselves spontaneously at puberty or in early adolescence, there are a sufficient number of cases in which testes will not descend and will atrophy. The avoidance of such atrophy and the psychic and physical handicaps which go with such a condition should warrant the institution of early treatment.

SUMMARY AND CONCLUSION

Fourteen boys, ranging in age from 6 to 13½ years, who presented maldeveloped or maldescended testes and were treated with the anterior pituitary-like gonadotropic hormone were made the basis for study in a previous report.

As a result of sufficient therapy with the anterior pituitary-like hormone, the genital tract in eleven patients of this series responded markedly by enlargement of the testes and by development of the external genitals.

The present paper reports further observations and additional data on the same series, namely:

Patients with adiposogenital dystrophy are subdivided into two groups—those with hypothyroidism and those with hypogonadism—depending on what is believed to be the gland primarily responsible for the genital underdevelopment. Additional subdivisions are suggested for clinical use.

Prolonged and intensive treatment with the anterior pituitary-like gonadotropic hormone is a requisite for a complete anatomic and physiologic result.

The testes of a young child usually increase in size only within the physiologic limits of the patient's age.

However, in a boy who is of pubertal age, hypoplastic testes seem to be able to enlarge in size beyond the normal limits for the age of the boy.

The enlargement of the penis, the formation of the scrotum, the enlargement of the epididymis and the development of pubic hair and the other sex accessories all seem to be conditioned by the proper stimulation of the testis, for the sex accessories do not develop until the testis itself begins to supply the male hormone in sufficient quantity to stimulate the accessory sex organs.

Overstimulation with the anterior pituitary-like hormone will cause precocious development of the external genitals and the secondary sex accessories in young boys.

Maldeveloped testes felt anywhere along the inguinal canal in almost all cases can be made to enlarge and descend. Often a testis that is seemingly not felt after repeated examinations may be found to appear

as a mushy mass after the institution of treatment, and its development then follows as it enlarges into a definite form and descends. The exceptions are, perhaps, the few cases in which cryptorchidism is due to a mechanical obstruction.

Treatment with the anterior pituitary-like hormone apparently produces no ill effects on the other organs of the body, and no mammary enlargement, nodulation or facial or general hirsuties directly due to this hormone has been noted.

The increment in height for the period of treatment with the anterior pituitary-like hormone was greater than that observed in the patients prior to treatment, or at least it was equal to the increment which took place when some of the patients were given thyroid medication. It was, too, generally greater than the calculated optimum increment in height for a similar period in a normal patient.

The increase in weight was greater than the increase observed in the patient prior to treatment. There was a slight redistribution of the pads of fat, particularly in those who received previous thyroid therapy.

The osseous development, particularly in the patients with hypothyroidism who showed retardation, was not further depressed by treatment with the anterior pituitary-like hormone; in fact, some of the patients kept good pace with the advance in the chronological age—at least they did not increase the existing lag in osseous development. In two cases of hypothyroidism the lag during this period of treatment with anterior pituitary-like hormone was practically overcome and the osseous age was almost normal.

The normal osseous development in the group with hypogonadism was not disturbed (study limited).

Studies of the basal metabolism of the patients with hypothyroidism, made prior to treatment and during and after treatment, showed changes in the rate, but they were too irregular to be significant.

Cleancut evidence is lacking that under treatment with the anterior pituitary-like gonadotropic hormone the thyroid gland is secondarily stimulated.

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ROENTGEN-POSITIVE SERONEGATIVE INFANTILE CONGENITAL SYPHILIS

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PHILADELPHIA

In the year Jan. 1 to Dec. 31, 1934, at the Philadelphia General Hospital, where the incidence of syphilis among the pregnant women is 11.8 per cent, not one of the 1,517 babies discharged alive from the maternity division showed any clinical evidence diagnostic of congenital syphilis. Of the 126 stillborn infants and infants dying soon after birth in this hospital in the same period of time, 19 (15.1 per cent) were the offspring of syphilitic mothers, the death rate being 9.7 per cent among the syphilitic group (195 patients) as compared with 7.5 per cent among the infants in the obstetrical division at large (1,643 patients).

It so happens that the majority of the syphilitic mothers who deliver their babies in this hospital have had insufficient treatment to insure the birth of healthy children, since it is unusual for a woman to report for prenatal supervision prior to the sixth month of her pregnancy, and she may come later than this. The most that we at this hospital can hope to do by treatment, therefore, in a large number of cases, is to prevent an unfortunate termination of the pregnancy in order to obtain a living and treatable child. The gratifying response of such infants to antisyphilitic therapy, when this is begun before the disease becomes clinically manifest, is well recognized.[1]

We have been interested, in this period of time, in evaluating the clinical practicability, as a diagnostic procedure in early infancy, of roentgenographic study of the skeletal changes produced by congenital syphilis in the offspring of partially treated mothers. Early congenital syphilitic osteochrondritis and periostitis have been studied from the roentgenopathologic point of view by a number of investigators,[2] and at

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From the Philadelphia General Hospital.

Presented before the Philadelphia County Medical Society, Feb. 27, 1935.

1. Sylvester, P. H.: Twenty-Five Years of Congenital Syphilis in Boston, J. A. M. A. **87**:298 (July 31) 1926. Rambar, A. C.: Syphilis and Prematurity, J. Pediat. **3**:841 (Dec.) 1933. Traisman, A. S.: Treatment of Congenital Syphilis with Acetarsone (Stovarsol) by Mouth, Am. J. Dis. Child. **46**:1027 (Nov.) 1933. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1934, chap. 22, p. 1281.

2. (*a*) Shipley, P. G.; Pearson, J. W.; Weech, A. A., and Greene, C. H.: X-Ray Pictures of the Bones in the Diagnosis of Syphilis in the Fetus and in Young Infants, Bull. Johns Hopkins Hosp. **32**:75 (March) 1921. (*b*) Turnbull,

autopsy the specificity of these bone lesions has been established by the demonstration of spirochetes [3] in the skeletal defects detected by roentgenogram before postmortem examination. The unreliability of serologic examination of such infants has been demonstrated by many workers [4] In 14 of the cases with which the present study is concerned the Kahn or Wassermann reactions of blood from the umbilical cord were positive, all in seropositive mothers; in 5 of these cases the infants became seronegative in less than ten days, demonstrating, I believe, the direct transfer of complement-fixing substance from mother to child.[5] If one admits, then, the unreliability, as an absolute diagnostic criterion, of the serologic examination of blood from the umbilical cord

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H. M.: Recognition of Congenital Syphilitic Inflammation of the Long Bones, Lancet **1**:1239 (June 24) 1922. (*c*) Pendergrass, E. P., and Bromer, R. S.: Congenital Bone Syphilis: Preliminary Report; Roentgenologic Study with Notes on Histology and Pathology of the Condition, Am. J. Roentgenol. **22**:1, 1929. (*d*) Bromer, R. S.: Osteochondritis Luetica: Comparison with Analogous Zones in Rickets and Infantile Scurvy, New England J. Med. **200**:524 (March 14) 1929. (*e*) O'Reilly, A.: Bone and Joint Syphilis, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 5, p. 215. (*f*) McLean, Stafford: The Roentgenographic and Pathologic Aspects of Congenital Osseous Syphilis, Am. J. Dis. Child. **41**:130 (Jan.); 363 (Feb.); 607 (March); 887 (April); 1128 (May) 1931. (*g*) Pick, L.: Zur Roentgendiagnose der angeborenen Knochensyphilis, Deutsche med. Wchnschr. **45**:953 (Aug. 28); 989 (Sept. 4) 1919. (*h*) Fraenkel, E.: Die kongenitale Knochensyphilis im Roentgenbilde, Hamburg, Lucas, Gräfe & Sillem, 1911. (*i*) Alexander, quoted by McLean.[2f] (*j*) Wimberger, quoted by McLean.[2f] (*k*) Hochsinger, Carl: Die Besonderheiten der kongenital-syphilitischen Erkrankungen der inneren Organe einschliesslich des Zentralnervensystems und des Bewegungsapparates, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 19, p. 116. (*l*) Péhu and Chassard: Schéma nosologique des ostéopathies syphilitiques observées dans la première enfance, J. méd. franç. **16**:427 (Nov.) 1927. (*m*) Brochier, André: Considérations anatomiques sur la syphilis du squelette des os longs chez le foetus, Rev. franç. de gynéc. et d'obst. **28**:204 (April) 1933.

3. Klug, G. F.: Finding of Spirocheta Pallida in Osteomyelitis by Dark Field Examination, with Report of 3 Cases, J. M. A. Georgia **13**:43 (Feb.) 1924. Hochsinger.[2k] Péhu and Chassard.[2l]

4. (*a*) Sylvester, P. H.: Discussion on Bromer.[2d] (*b*) Veeder, B. S., and Jeans, P. C.: Hereditary Syphilis, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 5, p. 611. (*c*) Roberts, M. H.: Congenital Syphilis, Am. J. Dis. Child. **45**:461 (March) 1933. (*d*) Williams, J. W.: The Value of the Wassermann Reaction in Obstetrics, Based upon the Study of 4,547 Consecutive Cases, Bull. Johns Hopkins Hosp. **31**:336 (Oct.) 1920. (*e*) Ingraham, N. R., Jr., and Kahler, J. E.: The Diagnosis and Treatment of Syphilis Complicating Pregnancy, Am. J. Obst. & Gynec. **27**:134 (Jan.) 1934. Shipley et al.[2a]

5. Rietschel, Hans: Allgemeine Pathologie der angeborenen Syphilis, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskranheiten, Berlin, Julius Springer, 1927, vol. 19, p. 1. Atlee, E. D., and Tyson, R. M.: Congenital Syphilis: Results of Early Treatment, Am. J. Dis. Child. **44**:718 (Oct.) 1932.

(Shipley et al.[2a] and Williams [4d]) the present series of 134 selected cases includes only 9 in which the diagnosis of congenital syphilis was suggested by routine physical examination and serologic study before the x-ray films revealed lesions of the bones. In this same group roentgenographic evidence of bone changes which have been described as characteristic of congenital syphilis was found in 49 cases (36.5 per cent)—in 26 cases (19.4 per cent) at the age of 6 days, before discharge from the maternity division, and in 23 additional cases (17.1 per cent) at ages from 1 to 10 months.

I mentioned the fact that the cases studied by means of the roentgen rays were selected. They were selected in the following sense: In making routine roentgenographic studies of the offspring of all syphilitic mothers, it became evident quite early that it was extremely uncommon to find evidence of bone syphilis in the x-ray film at 6 days when the mother had received more than two months of prenatal treatment. Thus, of the 26 cases in which such evidence was found before the child was discharged from the maternity division, in 5 the mothers had received no treatment at all; in 13, less than one month's treatment, and in 21, less than two months' treatment. Of 51 cases in which the mothers were treated more than two months, in 5 cases (9.8 per cent) there was roentgenographic evidence of the disease in the infant at 6 days, while of 68 cases in which the mothers were treated less than two months, in 21 (30.8 per cent) there was positive roentgenographic evidence of syphilis in the offspring. To reduce the expense of the procedure, therefore, the offspring of mothers who had received more than two months' prenatal treatment were studied at ages from 2 to 6 months rather than earlier. Of 36 cases adequately followed, in 12 (33 per cent) the roentgenograms subsequently became positive.

Most writers on the subject up till now have concerned themselves with demonstrating the specificity of the bone lesions of congenital syphilis by studying roentgenographically or pathologically the skeletons of infants proved syphilitic by clinical study. At the Philadelphia General Hospital we have tried to show the value of such study where other studies have failed to make the diagnosis. A few cases of roentgen-positive seronegative congenital syphilis have been reported by Shipley and his co-workers,[2a] Lindsay,[6] McLean [2f] and Vogt.[7]

Although the advanced bone changes which have occurred when the child is so severely diseased that it is stillborn or dies within the first few weeks of life are easily demonstrated roentgenographically, as McLean [2f] and Fraenkel [2h] have shown, the less marked osteochondritis which develops before the disease becomes clinically manifest has been

6. Lindsay, J. W.; Rice, E. C., and Selinger, M. A.: Bone Changes in Congenital Syphilis, Am. J. Syph. **11**:119 (Jan.) 1927.

7. Vogt, E. C.: The Value of Roentgenography in the Diagnosis of Congenital Syphilis, Am. J. Roentgenol. **26**:96 (July) 1931.

found much more difficult to recognize, especially when one is dealing with the offspring of partially treated mothers. Thus, Bell (mentioned by Hemsath[8]) of the New York Lying-in Hospital found roentgenographic examination at the age of 1 week of no great diagnostic value. Investigators at the Johns Hopkins Hospital,[9] examining their infants suspected of syphilis at the age of 14 days, found the roentgenogram of value in about 8 per cent of the cases, a result somewhat inferior to ours even though the children were a week older. Variations in the type of material and the amount of prenatal treatment may account for some difference between the two series. In cases 2, 3 and 4, the reports of which follow, I have endeavored to show the specificity of the early bone lesions (1) by comparing the bones with those of normal infants at the same age (typified in case 1) and (2) by showing, in serial studies, the development of the bone lesions in untreated syphilitic children until the Wassermann reaction became positive (cases 3 and 4) and until the advanced osteochondritis and periostitis left little doubt as to their nature. Although the bones of the forearm alone are shown, other portions of the skeleton show similar defects, as the roentgenographic descriptions with the case reports show. The four remaining cases show the remarkable value, at times, of roentgenograms in detecting congenital syphilis in slightly older infants when clinical and serologic evidence has failed to clinch the diagnosis.

REPORT OF CASES

CASE 1.—*A Normal Control Child (M. W.).*—Syphilis was excluded by the negative history and by the results of the physical examination of the mother, a 25 year old colored woman. Two previous pregnancies resulted in apparently normal children, now 11 years and 2 years old, respectively, and well. The maternal Kahn reaction was negative on Oct. 25, 1933, when she was five months pregnant, and on Feb. 12, 1934, at the time of delivery. The Kahn reaction of the blood of the umbilical cord was negative.

X-ray pictures were made of the long bones, carpal bones (fig. *A*) and tarsal bones of the infant at 6 days. The periosteal sufaces of all the long bones were sharply outlined. There was no evidence of increased calcification in the metaphyses of the radius, ulna, femur, tibia, fibula, carpal bones and tarsal bones.

CASE 2.—*An Infant (E. B.) Showing Typical Osteochondritis at the Age of Twenty-One Days; Advancement of Lesions at Three and One-Half Months.*—The mother had had more than one year's treatment. The child was seronegative.

The mother, a 17 year old colored girl, was discovered to have active syphilis at another hospital two years earlier and had one year's continuous treatment. When she reported for supervision of her pregnancy in the sixth month, the Kahn reaction was 1+; the reaction with cholesterolized antigen was negative; the Noguchi test was negative. Prior to delivery she had three injections (0.8 Gm.)

8. Hemsath, F. A.: A Study of the Wassermann Reaction in Pregnancy and Early Infancy, Am. J. Syph. **15**:396 (July) 1931.

9. McKelvey, J. L., and Turner, T. B.: An Analysis of the Outcome of Pregnancy in Relation to Syphilis in 943 Cases, J. A. M. A. **102**:503 (Feb. 17) 1934.

of neoarsphenamine and five injections (10 cc.) of bismuthyl salicylate. At the time of delivery the Kahn reaction was 3+; the reaction with cholesterolized antigen, 4+; the Noguchi reaction, 1+. The Kahn reaction of blood from the umbilical cord was negative. Serologic tests on the infant's blood were negative.

X-ray pictures made at 3 weeks showed a wide band of sclerosis in the metaphyses with a narrow band of submetaphyseal rarefaction and a second irregular band of diaphyseal sclerosis in the radius, ulna, femur, tibia, fibula and ilium bilaterally (fig. 1*B*).

At 3½ months (fig. 1*C*) the sclerosis was more prominent in the metaphyses of all the long bones, and the submetaphyseal rarefaction was more marked. There was spur formation of the distal radial and ulnar metaphyses. Periostitis was present on the inner aspect of the ulna. There was osteoporosis of the tarsal bones.

CASE 3.—*An Infant (R H.) Showing Progressive Development of Bone Lesions at Six Days, Two Months and Three and One-Half Months.*—At the last

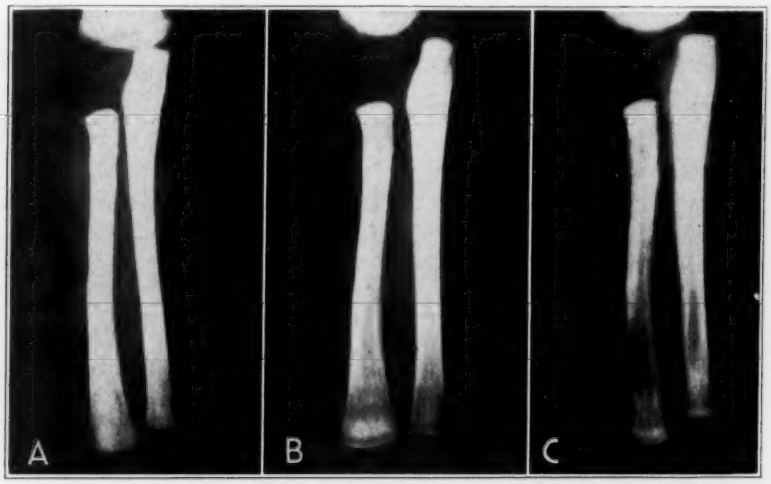

Fig. 1.—Right radius and ulna: *A*, of a normal child 6 days old; *B*, of the offspring of a syphilitic mother, at the age of 21 days, showing osteochondritis in the distal radial and ulnar metaphyses; *C*, of the same syphilitic child at the age of 3½ months, showing advancement of the lesion with flaring of the ends of the bones, widening of the zone of temporary calcification and increased submetaphyseal rarefaction. This child was seronegative and untreated.

mentioned age the child was found to have a positive Wassermann reaction of the blood and perianal lesions in which spirochetes were shown to be present by dark-field examination.

The mother of this child, a 24 year old colored woman, contracted a primary genital lesion in December 1933, when she was three months pregnant, and when she reported to the prenatal clinic in March 1934 she had annulopapular secondary lesions of the face of one month's duration. Her blood serum gave strongly positive reactions with three antigens. She received eight injections (3.45 Gm.) of neoarsphenamine prior to delivery, at which time the Kahn reaction was 1+, the reaction with cholesterolized antigen was 1+, and the Noguchi reaction was negative. The child was clinically normal at birth, June 13, 1934, and blood from the umbilical cord gave a negative Kahn reaction. At the age of 2 months,

August 7, generalized lymphadenopathy developed, and the liver and spleen became palpable. At 3½ months, September 25, perianal lesions were present in which dark-field examination showed spirochetes to be present; the Kahn reaction was 4+; the reaction with cholesterolized antigen was 4+; the Noguchi reaction was 4+.

An x-ray picture made at 6 days (fig. 2*A*) revealed periostitis on the inner aspect of the right ulna. (Localized periostitis in congenital syphilis has been especially mentioned by Landa and Panov.[10]) There was slight sclerosis in the distal radial metaphyses bilaterally. The distal metaphyses of both femurs showed a band of sclerosis, with a narrow band of submetaphyseal rarefaction proximally. There was osteoporosis of the small bones of the feet.

At 2 months (fig. 2*B*) there was a progression of the periostitis on the right ulna, with more marked sclerosis in the distal metaphyses of the radii and ulnas and some rarefaction in the distal portions of the diaphyses. Sclerosis was present in

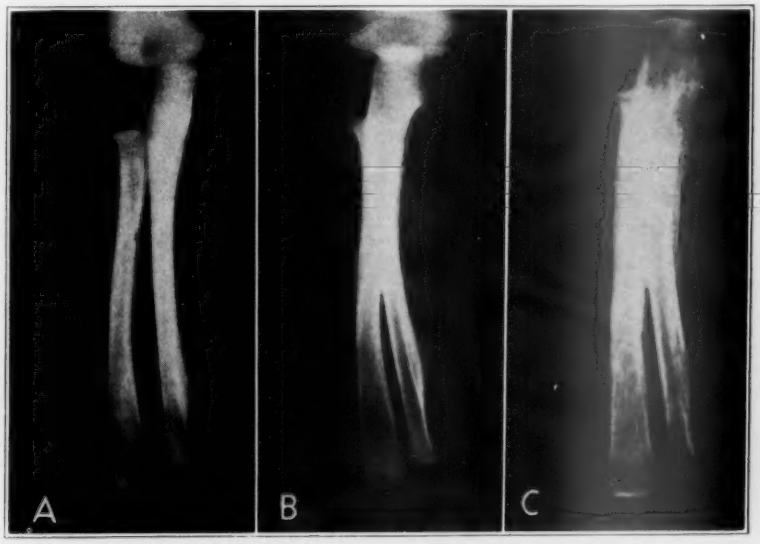

Fig. 2.—Right radius and ulna of a syphilitic child: *A*, at 6 days; *B*, at 2 months; *C*, at 3½ months. The roentgenograms show progressive development of a periosteal lesion on the inner aspect of the ulna and advancing osteochondritis in the metaphyses. In *A* there is a very narrow band of metaphyseal sclerosis with an equally narrow band of submetaphyseal rarefaction. This has increased tremendously in *C*.

the distal metaphyses of the tibias and fibulas with marked submetaphyseal rarefaction. There was rather marked osteoporosis of the small bones of the feet.

At 3½ months (fig. 2*C*) there were marked periostitis and osteochondritis of all the long bones.

CASE 4.—*An Infant (G. B.) Showing Progressive Bone Changes at Six Days, Two Months and Five Months.*—At the age of 5 months the Wassermann reaction became positive. At 5 months also the films showed what was probably an associated rickets, exemplifying the fact that this condition is prone to develop earlier in congenitally syphilitic children.

10. Landa, G. J., and Panov, V. P.: Matériaux pour le roentgéno-diagnostic de la syphilis congénitale, Ann. de dermat. et syph. **1**:867 (Aug.) 1930.

The mother, a 15 year old Negress, had negative serologic tests when she was six months pregnant, but at the time of delivery she was observed to have healing secondary lesions. At this time her Wassermann reaction and that of blood from the umbilical cord were both strongly positive. The child showed no abnormality at the time of birth (April 14, 1934) except gonococcic conjunctivitis; serologically it exhibited Menten's phenomenon,[11] being seronegative as late as May 28, when it was 6 weeks old. Its serologic tests were again strongly positive on September 4, when it was 4¾ months old. It commenced to show clinical signs of syphilis—snuffles and enlargement of the liver and spleen—when it was 2½ months old.

An x-ray picture made at 6 days (fig. 3*A*) disclosed a narrow band of sclerosis at the distal metaphyses of both bones of the forearm with a narrow band of rarefaction proximally. A similar picture was seen in the distal metaphyses of both femurs.

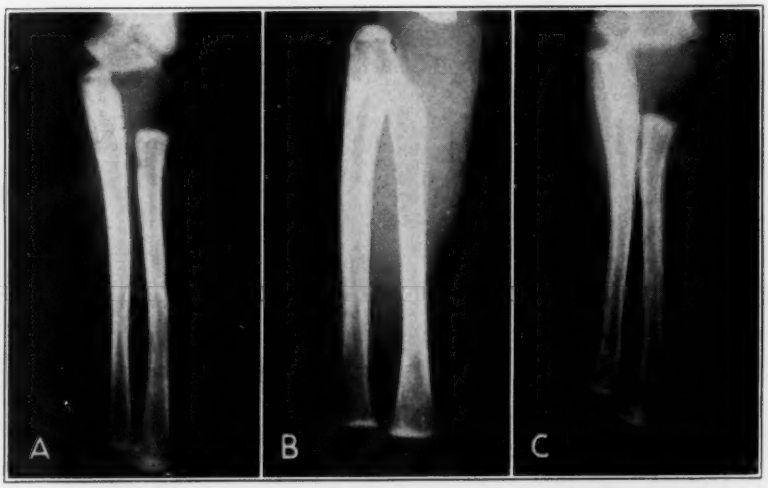

Fig. 3.—Left radius and ulna in an untreated syphilitic child: *A*, at 6 days; *B*, at 2½ months; *C*, at 5 months. The roentgenograms show progressive development of bone lesions. In *A* there is an irregular band of metaphyseal sclerosis; in *B* this has become more marked, while in *C* there are flaring, cupping and quite advanced periostitis.

At 2½ months (fig. 3*B*) there was a wide band of increased density in the metaphyses of all the long bones with submetaphyseal rarefaction. This change is most marked in the radii, ulnas and femurs.

At 5 months (fig. 3*C*) there was marked periostitis of the radius, ulna, femur and tibia, with flaring, cupping and sclerosis of the metaphyses of all the long bones. There was nuclear formation in the tarsal bones.

CASE 5.—*A Three Month Old Baby (D. W.) with Roentgen-Positive Seronegative Congenital Syphilis; Dark Field Positive; Maternal Wassermann Reaction Negative.*—The mother had negative serologic tests, was never known to have syphilis and was never treated. She was separated from her husband, and no data on him were available. The child had snuffles, perianal lesions in which dark-field

11. Menten, M. L.: A Positive Wassermann Reaction Which Changes to Negative at the Termination of Pregnancy, Am. J. Obst. & Gynec. **78**:514, 1918.

examination showed the presence of spirochetes, a negative Kahn and a negative Wassermann reaction (two antigens), and died of bronchopneumonia at the age of 5 months in spite of treatment.

X-ray pictures taken at 3 months (fig. 4) revealed a pathologic fracture of the left radius and flaring sclerosis of the metaphyses of all the long bones, with marked irregularity in the deposition of calcium salts. Periostitis was quite evident on the femur and tibia.

CASE 6.—*Seronegative Syphilitic Mother; Seronegative Syphilitic Child (H. D.)*—Congenital syphilis became active in the child at the age of 3 months with advanced bone changes and positive serologic reactions. This case shows the type of error which may be expected from relying solely on the Wassermann reaction for the diagnosis of syphilis during pregnancy.

The mother of this child had secondary syphilis with strongly positive serologic reactions two years before she was seen at this hospital, and she received ten

Fig. 4.—Radius and ulna (*A*), femur (*B*), tibia and fibula (*C*) show advanced bone lesions in a seronegative syphilitic child of 3 months. Note the fracture of the left radius, the flaring ends of the long bones with spurring and metaphyseal sclerosis, and the periostitis, which is quite evident on the outer aspects of the radius and ulna, femur and tibia and on the inner and outer aspects of the fibula.

weekly intramuscular and intravenous injections. On March 13, 1934, when six months pregnant, she was serologically negative. The Kahn reaction of blood from the umbilical cord on June 24 was negative. The child showed dactylitis, cutaneous lesions, a large liver and a large spleen, as well as generalized lymphadenopathy on September 25 (at 3 months of age), at which time both the mother's and the child's Wassermann and Kahn reactions were strongly positive.

X-ray pictures made at 3 months (fig. 5) showed a band of sclerosis in the metaphyseal centers of ossification of all the long bones, with marked submetaphyseal rarefaction. There was a marked periosteal reaction amounting to a cloaking in the bones of the forearm and lower part of the leg. There was marked porosity of the tarsal bones.

CASE 7.—*Seronegative Syphilitic Mother; Seronegative Child (G. W.)*—The mother was discovered to have a 2+ Kahn reaction, a 3+ reaction with choles-

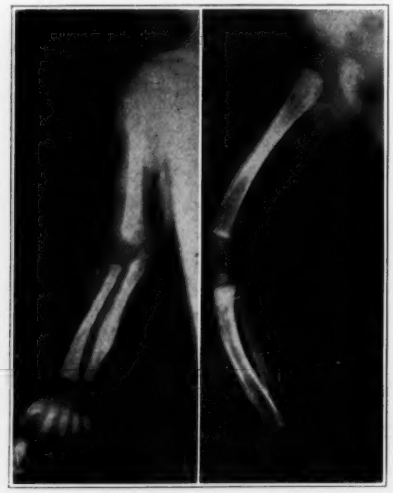

Fig. 5.—Long bones from the right upper and lower extremities of a 3 month old infant whose mother, though syphilitic, was seronegative during pregnancy and at the time of delivery. The roentgenogram shows marked universal osteochondritis and periostitis.

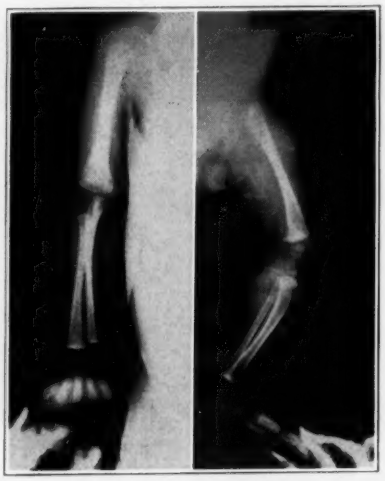

Fig. 6.—Right upper and left lower extremity of a 3 month old seronegative infant of a syphilitic mother. The roentgenogram shows increased metaphyseal sclerosis with flaring and spur formation of all long bones and periostitis on the outer aspect of the tibia.

terolized antigen and a negative Noguchi reaction Feb. 25, 1933, during the last preceding pregnancy, and she received four injections of neoarsphenamine and one injection of a bismuth preparation. On April 18, 1934, when she was again with a child and 4½ months pregnant, her Kahn reaction was negative; it was still negative at the time of delivery (September 9), as was the Kahn reaction of blood from the umbilical cord. She received four injections (1.1 Gm.) of neoarsphenamine during the latter pregnancy. The child began to have obstruction to nasal breathing at the age of 2 months (October 30) but was still seronegative.

An x-ray picture made at 6 days aroused a suspicion of congenital syphilis, as it showed sclerosis in the temporary zone of calcification in a distal femoral metaphysis, with submetaphyseal rarefaction.

At 2 months there were marked flaring and sclerosis of the distal metaphyses of the radius and ulna bilaterally. There was periostitis on the outer aspects of both femurs and both tibias (fig. 6).

Fig. 7.—Right upper and lower extremities of a 3 week old seronegative child with a family history of syphilis only. Note the double band of sclerosis in the distal radial and ulnar metaphyses separated by a line of rarefaction, the advanced osteochondritis in the femur, tibia and fibula, and the nuclear formation in the small bones of the feet.

CASE 8.—*A Hydrocephalic Child (J. R.) with Osteochondritis at the Age of Twenty-One Days While Seronegative; Seronegative Parents; Father Known to Have Been Syphilitic.*—The father, some years after marriage and eight years before the birth of this child, had a penile chancre for which he received about two years' treatment. The mother had never been known to be syphilitic and had never had treatment. Both parents had negative serologic reactions on Aug. 20, 1934, when the child was 3 weeks old, as had the child. The child died of pneumonia, hydrocephalus and spina bifida a short time later while serologic tests were still negative.

X-ray pictures at 21 days (fig. 7) showed advanced osteochondritis of all the long bones with definite sclerosis in the metaphyses and a wide zone of submetaphyseal rarefaction. Nuclear formation in the tarsal bones was beautifully shown.

SUMMARY

In the year from Jan. 1 to Dec. 31, 1934, at the Philadelphia General Hospital, even though the incidence of syphilis among the pregnant women was 11.8 per cent, and the majority of the patients received insufficient prenatal antisyphilitic therapy to insure the birth of healthy children, not one of the 1,517 babies discharged alive from the maternity ward showed any clinical evidence of congenital syphilis. The Wassermann reaction was of value in diagnosing syphilis in not more than 9 syphilitic children among 195 offspring of syphilitic mothers. The roentgenogram discovered 40 additional cases, 26 (19.4 per cent) before the age of 6 days and 23 cases (17.1 per cent) at ages from 1 to 10 months. In all of these cases the initial skeletal changes were evident roentgenographically before the blood serum gave a positive reaction.

Treatment of the mother prior to delivery affects the early roentgenographic evidence as follows: Of 51 cases in which the mothers were treated more than two months, in 5 (9.8 per cent) syphilis was shown in the infants roentgenographically at 6 days; of 68 cases in which the mothers were treated less than two months, in 21 (30.8 per cent) there was positive roentgenographic evidence of syphilis in the offspring. Cases in which the x-ray pictures revealed no positive signs at the age of 6 days were studied at ages from 3 to 6 months. Of 36 cases adequately followed, in 12 (33 per cent) the roentgenographic evidence subsequently became positive.

In 3 cases serial roentgenograms of the same child taken over a period of several months are shown, leaving no reasonable doubt that the earlier bone changes seen a few days after birth are the precursors of the more advanced and easily recognized bone lesions which developed subsequently. The Wassermann reaction which originally was negative became positive as the disease progressed, making a syphilitic etiology seem certain.

Case Reports

ACUTE MYELOGENOUS LEUKEMIA COMPLICATED BY NOMA AND ACUTE STREPTOCOCCIC DERMATITIS

N. FREDERICK HICKEN, MD.
AND
R. BRUCE ELDREDGE, M.D.
OMAHA

Acute myelogenous leukemia occurring prior to the age of 4 years is unusual. Noma, once quite common, is now a clinical curiosity. Generalized acute streptococcic dermatitis, formerly known as "hospital pemphigus," occurs infrequently. To find all three of these unusual but interesting conditions combined in one case seems to justify a report.

REPORT OF A CASE

History.—A Negro boy 3 years of age was admitted to the University Hospital because of "sore mouth."

When 9 weeks of age the child was brought to the university dispensary because of persistent coryza. Conservative treatment soon restored him to health. Periodic examinations indicated that he had had a normal development.

Three weeks before his admission to the hospital the child's mother noticed that both his ankles were swollen and edematous and that he walked with a peculiar limping gait. Examination revealed large, inflamed tonsils, diffuse bilateral cervical adenopathy and an inflammatory periarticular swelling of the hands, feet and ankles. Within one week all symptoms had disappeared except the cervical adenopathy. Apparently the mild inflammatory arthritis was precipitated by the tonsillar infection; therefore, it was advised that tonsillectomy be performed as soon as his general condition permitted. Unfortunately, no hematologic studies were made at the dispensary.

Two weeks later, while chewing gum, the patient bit the inner surface of the right cheek. Within two days the entire cheek was swollen, painful and edematous. Four days after the original trauma, his breath was very offensive, and on examination his mother found a large sloughing ulcer involving the inner surface of the right cheek. Local treatment, such as hot packs and irrigations of the mouth, were ineffectual, as was indicated by the rapid extension of the ulcer.

Examination.—The patient was well nourished. The temperature was 101.3 F., the pulse rate 120 and the respiratory rate 18. The right cheek, the right half of the upper lip and the right side of the nose were involved in a firm, tense inflammatory swelling. Palpation showed the entire cheek to be firm and indurated but not tender. On the inner surface of the cheek was a large sloughing ulcer which was covered with gray necrotic membrane. The membrane could be

From the University of Nebraska College of Medicine.

removed easily, leaving a gangrenous, nonbleeding base. The ulcer spread both by peripheral extension and by direct invasion of the soft tissues of the cheek. The gums were swollen and tender, but there were no areas of bleeding or ulceration. The tonsils were enlarged, and inspissated plugs of material could be expressed from the tonsillar crypts. The breath had a repulsive, fetid odor.

There was generalized cervical adenopathy. The glands were firm, hard, discrete and movable. The inguinal and epitrochlear glands were moderately

Fig. 1.—Early stage of noma, showing the marked inflammatory edema and swelling of the cheek, nose and lips. The skin is intact.

Fig. 2.—The gangrenous stage of noma. Note the complete perforation of the cheek and the induration and swelling of the tissues surrounding the necrotic ulcer.

enlarged. The liver extended 1 inch (2.5 cm.) below the right costal margin; it was smooth and not tender. The spleen could not be palpated.

On admission to the hospital the blood showed 5,200,000 erythrocytes, with a hemoglobin percentage of 73. There were 44,500 leukocytes, with a differential count of 43 per cent segmented polymorphonuclears, 10 per cent staff forms, 12 per cent young forms, 5 per cent myelocytes, 1 per cent promyelocytes, 10 per cent lymphocytes, 15 per cent monocytes, 2 per cent blast cells and 2 per cent unidentified forms. Forty-four normoblastic and other immature red cells were

encountered while making the differential count of 100 leukocytes. Fifty-nine per cent of the white cells gave a positive reaction for oxidase. On the basis of these observations it was thought that the patient had acute myelogenous leukemia complicated by ulcerative stomatitis.

Treatment and Course.—Active treatment was immediately instituted. The oral cavity was frequently irrigated with oxidizing solutions, such as potassium permanganate and sodium perborate. Both moist and dry heat were applied every two hours. Neoarsphenamine was administered intramuscularly. Several transfusions of whole blood were given in an attempt to reenforce the patient's general resistance. In spite of this active therapy the ulceration spread rapidly. The patient became very toxic; the pulse rate increased to 130, and the temperature varied between 101 and 100 F.

On the fourteenth day after the patient's admission to the hospital the right side of the face was intensely swollen, and the brawny induration had increased. The

Fig. 3.—The nomatous ulcer has been excised, and mucosa is rapidly covering the denuded areas.

skin overlying the central portion of the inflammatory tumor had a peculiar brownish discoloration, which rapidly became black and gangrenous and finally perforated. This large foul-smelling, gangrenous, perforating ulcer, which permitted the constant drooling of saliva, combined with the extensive inflammatory swelling of the face, presented a gruesome sight.

On the thirty-ninth hospital day the patient was seen in surgical consultation (N. F. H.), and it was believed that even in the presence of leukemia the necrotizing ulcer should be excised, not because it could influence the course of the leukemia but because excision of the decomposing tissue would make nursing care more pleasant and at the same time reduce the toxemia due to absorption. With the patient under avertin anesthesia all the diseased tissue was removed by cautery excision. Extreme care was taken to see that only healthy tissue remained. The entire right side of the cheek and a portion of the upper and lower lips were removed. The periosteum and cortical portion of the maxilla were diseased, and this infected tissue was removed by curettage. Hot packs and frequent irrigation soon stimulated the formation of healthy granulation tissue.

The child gave an excellent response until the ninth postoperative day, at which time he contracted an acute streptococcic sore throat and laryngitis which finally developed into bilateral bronchopneumonia. He seemed unable to combat this widespread systemic infection, as his resistance was low. Seventeen days after the first operation it was again necessary to excise a portion of necrotic gingival tissue from both the maxilla and the mandible and to extract four teeth. The diseased bone was carefully curetted. The ulceration, however, continued, and for

Fig. 4.—Acute streptococcic dermatitis involving the face, ear, neck, chest and abdomen. No areas of ulceration are seen. There is no evidence of noma.

a third time the gangrenous portion of the cheek and lip were excised, a considerable amount of healthy tissue being sacrificed. During the remainder of hospitalization there was no recurrence of the noma.

On the twenty-second postoperative day a small vesicle appeared on the inner surface of the left ear. Five hours later the entire ear was covered by a large "blister." The epidermis was separated from the dermis by clear yellow fluid. When the top of the vesicle was removed the dermis appeared very red and

hyperemic. No ulceration or formation of abscess was seen. Forty-eight hours later, the inflammatory reaction had subsided and the process of healing had begun.

Soon several small blebs appeared in the suprasternal notch, and within six hours the entire right side and posterior aspects of the neck were covered by one huge "blister." A pure strain of streptococci was grown from the vesicular fluid. Five days later several small vesicles were seen in the interscapular area. These became confluent and extended peripherally until the entire trunk was covered by one huge bulla. Nonhemolytic streptococci were recovered from these lesions. Careful examination of the hyperemic dermis failed to show ulceration, gangrene or necrosis of the tissue.

The patient died on the thirtieth postoperative day of acute myelogenous leukemia, bronchopneumonia and acute streptococcic dermatitis. There was no evidence of the preexisting noma; in fact, the oral mucosa was beginning to cover the denuded area.

COMMENT

Acute Myelogenous Leukemia.—Both the chronic and the acute forms of lymphatic and myelogenous leukemia are uncommon during infancy and early childhood, few cases having been recorded. Acute myelogenous leukemia has been reported as occurring in a baby 3 weeks of age by White and Burns,[1] in one 5 weeks old by Giblin [2] and in one 5 months of age by Salmonsen.[3]

These acute myeloid disturbances may present difficult diagnostic problems, often requiring postmortem studies to unravel the puzzle. Our patient first had generalized inflammatory arthritis, tonsillitis and ulcerative stomatitis, all of which helped to obscure the leukemic process. Accompanying these inflammatory reactions was a generalized adenopathy associated with a leukocyte count of 44,500 cells, 59 per cent of which gave a positive reaction for oxidase. It is true that the hematologic studies suggested leukemia, but after excision of the nomatous ulcer the total white cell count decreased to 19,000, and there was a sudden transition from the immature to the mature forms. In fact, there were 29 per cent mature lymphocytes and 43 per cent adult polymorphonuclears. The erythrocyte-forming elements were likewise responding to the hematopoietic stimulus, for there were 7,250 normoblastic and other immature erythrocytes per cubic millimeter of blood. This would suggest that the blood-forming tissues were making an abnormal response to some infectious stimulus (the noma) and that on removal of the stimulation the immature cells tended to revert to the mature forms. The absence of splenic enlargement and the failure

1. White, P. S., and Burns, F. L.: Fatal Acute Lymphoblastic Leukemia with Great Enlargement of the Kidneys in an Infant Three Weeks Old, Am. J. Dis. Child. **41**:866 (April) 1931.

2. Giblin, J.: Acute Myelogenous Leukemia in an Infant Five Weeks Old, Arch. Pediat. **50**:662 (Sept.) 1933.

3. Salmonsen, L.: Leucémie myélogène aigue chez un enfant de cinq mois, Acta pædiat. **9**:497, 1930.

of the mucous membrane to bleed, combined with this unusual hematopoietic response, made the diagnosis difficult. Necropsy studies revealed a generalized myelogenous infiltration of all the vital organs, particularly the liver, spleen and lymph nodes.

Cutaneous Eruptions Associated with Leukemia.—The leukemias are associated with a great variety of cutaneous lesions, some of which are part and parcel of the leukemic process while others are merely incidental. There are two types of true leukemia cutis. In one type abnormal leukoid cells infiltrate the skin and subcutaneous tissues, producing circumscribed leukemic nodules and tumors. This group has been accurately described by Barney.[4] In the other type there is generalized leukemic infiltration of the skin, forming the so-called "universal leukemia cutis" which Sutton [5] has observed. Montgomery [6] expressed the opinion that infiltration of the skin by the myeloid cells is a common occurrence in cases of acute myelogenous leukemia, and he advised biopsy on specimens of skin as an aid to diagnosis. We were unable to substantiate his contention.

The vast majority of cutaneous lesions associated with the various forms of leukemia are merely incidental. Systemic toxemia, coincidental infection and generalized debility usually account for these lesions. For example, the intractable pruritus accompanying leukemia is an expression of a toxic reaction, for the most meticulous histopathologic studies fail to show any abnormalities of the skin or its nerves. Acute myelogenous leukemia may be complicated by herpes zoster, as reported by Fischl;[7] by a generalized streptococcic cutaneous infection, as noted by Detlefsen;[8] by necrotic purpura resembling anthrax, as observed by Landias [9] and by urticaria, urticaria papulosa and multiple furuncles and carbuncles, as reported by Arndt.[10] To differentiate these associated lesions from true leukemic cutis, Audry [11] suggested the term leukemid and Cole [12] pseudoleukemia. The gangrenous stomatitis (noma)

4. Barney, R. E.: Leukemic Myelosis Associated with Specific Nodules in the Skin with Report of a Case and a Review of the Literature, Arch. Dermat. & Syph. **27**:725 (May) 1933.

5. Sutton, R. L.: Diseases of the Skin, St. Louis, C. V. Mosby Company, 1926.

6. Montgomery, quoted by Arndt.[10]

7. Fischl, F.: Leukemia with Generalized Herpes Zoster, Arch. f. Dermat. u. Syph. **118**:553, 1913.

8. Detlefsen, M.: Erysipelas-Like Cutaneous Manifestations of Myeloblastic Leukemia, Zentralbl. f. Chir. **60**:2303, 1933.

9. Landias, quoted by Weaver and Tunnicliffe.[16]

10. Arndt, G.: Skin Changes Accompanying the Lymphoblastomas, J. A. M. A. **63**:1268 (Oct. 10) 1914.

11. Audry: Ann. de dermat. et syph. **3**:452, 1882.

12. Cole, H. N.: The Cutaneous Manifestations of Hodgkin's Disease, with Report of Eighteen Cases: Discussion, Classification, Literature, Tr. Sect. Dermat. & Syph., A. M. A., 1917, p. 192.

and the streptococcic pemphigus seen in our case belong to the group of leukemids, as they were not true leukemic lesions.

Noma.—Clinically, noma is a progressive, phagedenic ulcer, usually involving the oral cavity. However, any part of the body may be involved. Holt [13] reported seven cases arising in the external ear from preceding chronic otitis media; Henoch [14] reported a case involving the labia and vulva and Bodin [15] had a patient with noma affecting the genito-anal region. Noma is usually associated with such diseases as measles, scarlet fever, typhoid, diphtheria, bronchopneumonia or leukemia. In fact, any disease which materially lowers the resistance of the patient may be a precursor of this ulcerative process.

Numerous organisms have been recovered from these gangrenous ulcers, all of which have been considered as causative factors. The fusiform bacillus, spirochete, streptococcus, staphylococcus, streptothrix, cladothrix and diphtheroid bacillus have been found most frequently. Weaver and Tunnicliffe [16] and Rona [17] expressed the opinion that the fusiform bacillus is the causative agent. Dr. Paul Bancroft, of the department of bacteriology, has made careful studies in this case. From the sloughing gangrenous area he cultured fusiform bacilli, spirochetes, nonhemolytic streptococci, Staphylococcus aureus, diphtheroid bacilli and gram-positive bacilli. From the zone of reaction, i. e., at the junction of the inflamed and gangrenous tissues, he found the anaerobic fusiform bacilli, anaerobic micro-aerophilic nonhemolytic streptococci and isolated groups of anaerobic staphylococci. Cultures of these combined organisms presented the same offensive fetid odor as did the gangrenous cutaneous lesion.

Histopathologic studies of the gangrenous portion of the ulcer showed that all cells had lost their morphologic identity. Their nuclei were pyknotic and fragmented, the walls of the cells had disintegrated and the entire mass of tissues stained homogeneously. In the zone of reaction there was a slight round cell infiltration but nothing to suggest a leukemic process. The walls of the blood vessels were slightly thickened, and their lumens were filled with obstructing thrombi. As one approached the normal tissue, the lumens of the vessels were patent but contained a number of disintegrating red blood corpuscles. Scattered throughout the zone of reaction were peculiar rod-shaped bacilli having

13. Holt, L. E.: Diseases of Infancy and Childhood, ed. 10, New York, D. Appleton & Company, 1920.

14. Henoch, E.: Vorlesungen über Kinderkrankheiten, ed. 5, Berlin, A. Hirschwald, 1890, p. 464.

15. Bodin, E.: Gangrène foudroyante des organes génitaux externes chez la femme, Presse méd. **36**:1611, 1928.

16. Weaver, G., and Tunnicliffe, R.: Noma, J. Infect. Dis. **4**:8, 1907.

17. Rona: Arch. f. Dermat. u. Syph. **67**:259, 1903.

rounded ends. These bacilli had invaded the skin and the subcutaneous tissues. They were often clumped together or arranged in palisade formation. The leukocytes had phagocytosed many of them. In other areas there were small groups and chains of cocci, some of which had been phagocytosed. In the peripheral zone, i. e., at the junction of the normal and diseased tissue, only a mild inflammatory reaction could be demonstrated. The blood vessels were engorged; the tissues were hyperemic, and the number of polymorphonuclears was increased.

Since it was impossible to demonstrate leukemic changes in the nomatous ulcer, it seemed evident that the changes were due to bacterial invasion and were not part of the leukemic process. This concept was supported by the fact that noma occurs as a complication of the other diseases. We have also accumulated experimental data which proves that in this case the noma was a phagedenic ulcer caused by a bacterial synergism of the fusiform bacilli, the anaerobic micro-aerophilic nonhemolytic streptococci and Staphylococcus aureus. While it is possible to have a symbiotic relationship of many bacteria, evidence indicates that the fusiform bacilli and the nonhemolytic streptococci are generally found in all nomatous lesions. Not much importance can be attached to reports of cases in which anaerobic and aerobic cultures have not been made. Detailed reports of our experimental work have appeared elsewhere.[18]

Since one knows that noma is an infective gangrene of the skin, one can immediately appreciate the fallacy of conservative therapeutic measures. Chemotherapy and local treatment of the necrotic ulcer are ineffective. Early radical excision of all the diseased tissue offers the best prognosis. The incisions must extend out into the normal healthy tissue so as to get beyond the area of active inflammation.

Radical excision of a large nomatous ulcer, particularly if it involves the face, results in hideous deformities. Conservative measures invite a recurrence of the ulcer. Therefore, we think it advisable to make a wide excision of all diseased tissue and repair the deformities at a later date. Reconstructive work should be delayed two or three months after all infection has subsided. Usher and Ross[19] successfully repaired the facial deformities of a patient who recovered from typhoid and noma. Duhail[20] cured a patient with advanced noma by thermocauterization

18. Hicken, N. F.: Infectious Gangrene of the Skin Due to Bacterial Synergism, with Particular Reference to Noma and Postoperative Cutaneous Gangrene, Arch. Surg. **31**:253 (Aug.) 1935.

19. Usher, S. J., and Ross, D. E.: Cancrum Oris Following Typhoid Fever with Plastic Repair: A Case, Canad. M. A. J. **25**:446 (Oct.) 1931.

20. Duhail: Noma: Early Thermocauterization and Antigangrenous Sero-Therapy Followed by Recovery, Bull. et mém. Soc. de chir. de Paris **25**:620 (Nov. 3) 1933.

and antigangrene serotherapy. Pollosson and Lebeuf [21] successfully treated a patient with facial noma only to have the patient die a little later of lymphoid leukemia. Hence, even in hopeless cases it is advisable to excise the phagedenic ulceration, as it makes the nursing care more pleasant and reduces the systemic toxemia.

Acute Streptococcic Dermatitis.—"Hospital pemphigus," or acute streptococcic dermatitis, was formerly encountered frequently. Malnutrition, overcrowding, bacterial contagion and unsanitary conditions often permitted epidemics of this infection to spread rapidly through large hospitals. Today this disease is seldom seen.

The acute dermatitis began as a small yellow vesicle which advanced by peripheral extension. Adjacent lesions became confluent, and the vesicular eruption progressively spread from the ear to the neck and then to the abdomen. The epidermis had a peculiar shiny glaze and seemed to be floating on top of the yellow serous fluid. Nonhemolytic streptococci were grown from the serous exudate. When the epidermal covering was removed from the vesicle the dermis had a hyperemic, edematous appearance. No areas of formation of abscess, ulceration, necrosis or leukemic infiltration were seen. The excessive hyperemia of the dermis accounted for the rapid formation of the exudate. Four days after the vesicle had ruptured and the serous fluid had escaped the inflammatory process had practically subsided.

Why did not these large denuded streptococcic lesions undergo gangrenous changes? What prevented them from becoming nomatous ulcers? Why did they heal spontaneously when the noma would not? The apparent answer to these questions is that the acute dermatitis was caused by organisms of a single group, nonhemolytic streptococci, while it required the symbiotic relationship of nonhemolytic streptococci, fusiform bacilli and staphylococci to produce the necrotizing nomatous lesion. This postulate was confirmed by the observation that when the nonhemolytic streptococci were injected intradermally into rabbits and guinea-pigs invariably an acute localized dermatitis resulted. All such lesions healed spontaneously within one week. When, however, bacterial suspensions consisting of fusiform bacilli, Staph. aureus and nonhemolytic streptococci were injected, a large, sloughing, gangrenous ulcer of the skin and subcutaneous tissues occurred. These experimental results combined with the histopathologic studies of the noma conclusively proved that the noma and the acute streptococcic dermatitis were both due to an acute bacterial infection and were not part of the leukemic process.

21. Pollosson and Lebeuf, F.: A Cure of Noma by Antigangrenous Serum and Subsequent Appearance of Lymphoid Leukemia, Bull. Soc. franç. de dermat. et syph. **40**:1061 (July) 1933.

SUMMARY

An unusual case is reported of atypical acute myelogenous leukemia, occurring in a Negro boy 3 years of age, complicated by noma and streptococcic dermatitis.

Acute myelogenous leukemia in early childhood is unusual and often presents diagnostic difficulties.

Noma, or acute gangrenous stomatitis, is not caused by leukemic infiltration of the skin and mucous membrane but is acute infective gangrene. In this case the provocative organisms were fusiform bacilli, anaerobic micro-aerophilic nonhemolytic streptococci and Staphylococcus aureus. When a mixed bacterial suspension containing these three organisms was injected into the skin of the abdomen of a rabbit or guinea-pig, large phagedenic, sloughing, gangrenous ulcers of the skin and subcutaneous tissues appeared. This proves that noma is an infective gangrene caused by bacterial synergism.

The treatment of noma consists of early radical excision of all the diseased tissues. The resulting deformities can be repaired by plastic surgery after the infection has completely subsided.

Acute streptococcic dermatitis, or hospital pemphigus, is an active infection of the skin, in this case caused by nonhemolytic streptococci.

OPEN FORAMEN OVALE ASSOCIATED WITH MITRAL STENOSIS

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AND
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The presence of a defect of the interauricular septum in conjunction with mitral stenosis has been reported by a number of observers. McGinn and White [1] recently presented an excellent review of twenty-three previously reported cases and added one of their own. Since the publication of their report, two other cases have been recorded by Jerofejeff [2] and Mitchell and Bauer.[3] We have encountered an example of this condition which seems worthy of being placed on record, not only because the condition is rare but because our case offered a number of unusual features.

REPORT OF A CASE

H. A., a white boy, was born on March 31, 1923. He was the second of four children. An older brother is under observation because of a systolic murmur along the left sternal margin, suggestive of congenital cardiac disease. One other child, born prematurely, died at the age of 6 weeks and was cyanotic from birth. It was the opinion of the attending physician that the child had congenital cardiac disease. The parents were well. Examination of the mother showed an eccentric oval pupil of the left eye.

The patient was first admitted to the hospital on Oct. 30, 1924, at the age of 19 months, with a history of fever of a few days' duration and a convulsion two days previous to admission. From birth the baby had had attacks of cyanosis, shortness of breath and grunting respiration.

Physical examination revealed the presence of an infection of the upper respiratory tract. The cardiac examination showed slight bulging of the precordium, enlargement of the heart, a short systolic thrill and a loud, widely transmitted systolic murmur, maximum in the third left interspace. It was of interest that in addition to the evidence of congenital cardiac disease he had a congenital incomplete coloboma of both eyes and a "cobra" penis, with a small hypospadial opening.

From the Children's Memorial Hospital and the Otho S. A. Sprague Memorial Institute.

1. McGinn, Sylvester, and White, Paul D.: Interauricular Septum Defect Associated with Mitral Stenosis, Am. Heart J. **9**:1 (Oct.) 1933.

2. Jerofejeff, P.: Offenes Foramen ovale bei Mitralstenose, Frankfurt. Ztschr. f. Path. **46**:92, 1934.

3. Mitchell, W. G., and Bauer, J. T.: Interauricular Septal Defect Associated with Mitral Stenosis: Report of Case, Bull. Ayer Clin. Lab., Pennsylvania Hosp. **3**:29 (May) 1934.

Wassermann tests of the blood and spinal fluid gave negative results. The respiratory infection cleared up, and the patient was discharged from the hospital on Dec. 29, 1924.

He was again admitted to the hospital on July 26, 1926, because of shortness of breath and a distended abdomen. Several nights previously he had had a hard crying spell, during which he became cyanotic. Examination at this time revealed that the edge of the liver was 3 fingerbreadths below the costal margin. No change in cardiac findings was noted. With rest in bed the signs of heart failure disappeared, and the patient was discharged on Sept. 11, 1926.

His third admission occurred on Sept. 18, 1926, with a history of generalized pains in the joints of two days' duration. The temperature was 103.6 F. on admission, but promptly subsided. While in the hospital he contracted nasal diphtheria, and 20,000 units of antitoxin was given. An electrocardiogram obtained at this time showed right axis deviation. He was discharged from the hospital on March 9, 1927.

The child then was fairly comfortable until March 1, 1930, when he returned to the hospital with the complaint of a bad cold and earache. Physical examination at this time revealed the presence of pneumonia of the lower lobe of the left lung and bilateral otitis media. These conditions cleared, and he was discharged on April 17, 1930.

Following this, the child remained fairly well for over two years. He had been attending school and was able to exercise moderately without distress.

On Oct. 7, 1932, he came into the hospital for the fifth time, complaining of fever, cough, vomiting, earache and shortness of breath. He was found to have an infection of the upper respiratory tract. He was dyspneic and slightly cyanotic about the lips. The liver was markedly enlarged, and the spleen was easily palpable. Shortly after admission fibrillation developed, which persisted for a few days. He gradually improved and was discharged on March 22, 1933.

His sixth and final admission was on May 22, 1933. He had been coughing for a week; he had pain in the upper part of the abdomen and was unable to breathe comfortably lying down. At this time he was slightly cyanotic, and the margin of the liver was at the level of the umbilicus. On June 7, and again on August 22, he had typical circinate erythema. His course was steadily down-hill. Anasarca developed, and in spite of digitalis and diuretics his condition was not improved. Fibrillation again started. Two days before death he became extremely cyanotic, and he remained so until he died, on Nov. 1, 1933.

The postmortem examination was made one and one-half hours after death. The body appeared fairly well nourished and developed, measuring 130 cm. in length. The face was puffy, and pitting edema of the thoracic and abdominal walls, the sacrum and the dependent portions of the lower extremities was present. There was a bluish discoloration of the lips and nail beds. The fingers and toes showed a very slight clubbing. Both eyes showed coloboma of the iris. The penis was of the "cobra" type with glandular hypospadias.

The pleural cavities each contained about 250 cc. of clear amber-colored fluid; 2 liters of a similar fluid was present in the peritoneal cavity. There were fibrous pleural adhesions at the base of the right lung. The lungs, liver, spleen and kidneys showed signs of recent and chronic passive congestion. A small Meckel's diverticulum was located in the upper portion of the ileum.

The heart was enormous, weighing 410 Gm., the normal weight for this age being approximately 140 Gm. Its maximum transverse diameter in situ measured 15.5 cm., the thorax being 20.5 cm. across. There was a marked disproportion, the right chambers composing most of the heart and the left atrium and ventricle being atrophic by comparison. There were many small subepicardial hemorrhages; a smooth thickened area of epicardium ("soldier's patch") was located on the right ventricle near the apex, which was formed entirely by this ventricle. The large vessels had their normal relationships. The pulmonary artery was large, with a wall of normal thickness, having a circumference of 7.5 cm. just above its origin; the aorta was hypoplastic, with a circumference of 2.8 cm. (fig. 1). The ductus arteriosus was closed.

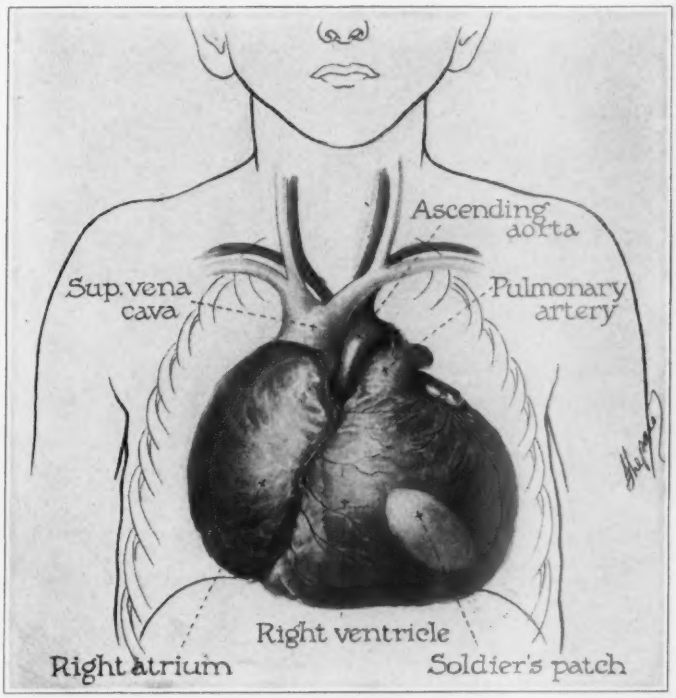

Fig. 1.—Appearance of the heart and of the great vessels in situ at autopsy, showing the large pulmonary artery, the small aorta and enlargement of the right atrium and ventricle.

On being opened the dilated right atrium was found to have a thickened wall. The interatrial wall presented a remarkable appearance because of a widely open foramen ovale. This was almost round, measuring 4 by 3 cm.; a thin, fenestrated valvula foraminis ovalis bound the posterosuperior margin of this opening and bulged slightly toward the right (fig. 2). The tricuspid leaflets were thickened and somewhat inelastic. The tricuspid ring measured 12 cm. The right ventricle was greatly dilated and had a considerably hypertrophied wall, 1.3 cm. in average width. The pulmonary valve was normal. Except for its large size, the pulmonary artery presented no unusual features.

The left atrium was relatively small. A patch of thickened, puckered endocardium was located on its posterior wall just above the mitral orifice. This mitral ring measured 6.8 cm. and appeared definitely stenotic. Both mitral leaflets were thick and stiff, with shortened coarse chordae tendineae; no rheumatic vegetations were seen on the leaflets of the mitral or other valves (fig. 3). The left ventricle was small. Its wall had an average thickness of 1.1 cm. Scarring was visible to the naked eye. The aortic valve measured 7.2 cm.; its semilunar cusps were delicate in appearance. As noted before, the aorta was small and had a thin

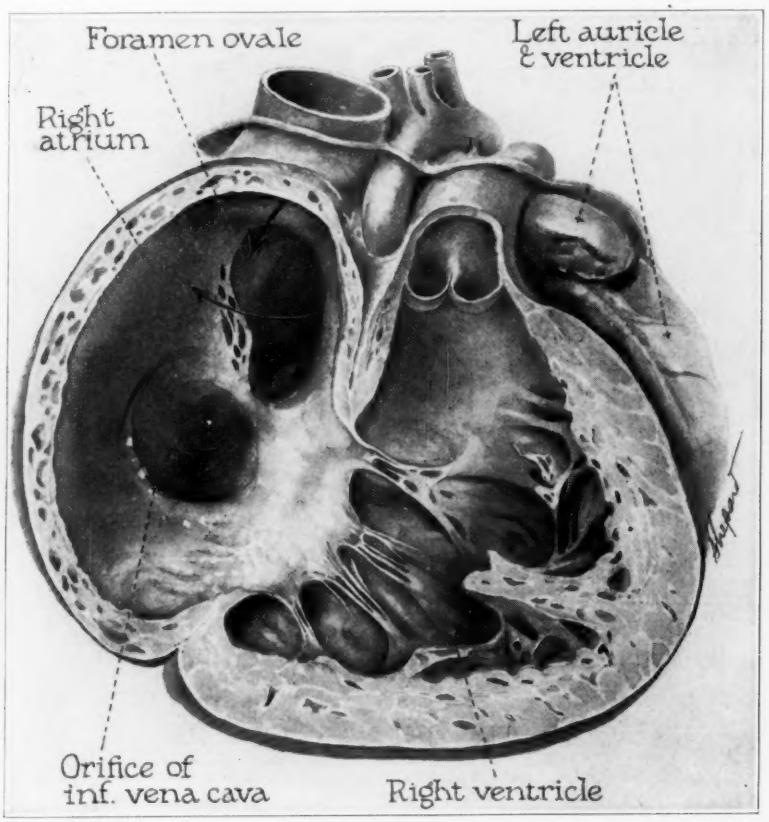

Fig. 2.—The opened heart as seen from the right side. Note the large patent foramen ovale and the middle arrow indicating the usual direction of the flow of blood through this opening.

wall in both its thoracic and its abdominal portion. The innominate, the left common carotid and the subclavian artery arose in their customary manner.

Microscopic examination of the heart showed a moderate number of typical fresh and old perivascular Aschoff bodies, with diffuse fibrosis; the myocardial fibers were hypertrophied, with large prominent nuclei.

Sections of the other organs showed a marked generalized venous congestion. Widespread central necrosis was present in the liver, which also had a slight periportal scarring.

REPORT OF A CASE FOR COMPARISON

Before proceeding with a discussion and interpretation of our own report, we wish to present the case of a patient observed by Dr. H. Gideon Wells, in which the history, the results of physical and post-mortem examinations and the roentgenogram contain many interesting and instructive points, affording a fortunate control for our own case.

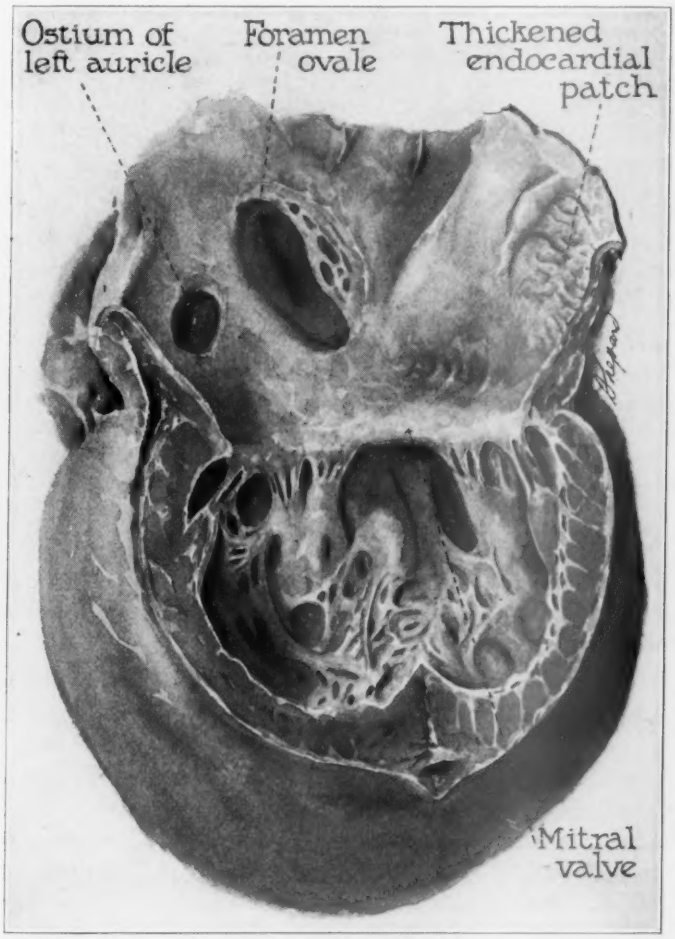

Fig. 3.—The opened heart as seen from the left side. Note the stenotic mitral valve and the small size of the left chambers.

M. L., a 25 year old Philippine caretaker, was admitted to Billings Hospital in December 1927, complaining of tachycardia. He had had a chronic cough and expectoration of a frothy material as long as he could remember. However, he had always played and exercised normally until the past year. For six months before entering the hospital he had suffered from nocturnal dyspnea. Examination

showed the left side of the chest to be bulging in both diameters, with a heaving apical impulse in the anterior axillary line in the sixth interspace; percussion showed that the right cardiac border was 11 cm. from the midsternal line in the fourth interspace. A loud systolic murmur was heard over the heart, loudest in the third left interspace, accompanied by a systolic thrill. There was a questionable late diastolic murmur. The fingers were slightly clubbed, and signs of moderate myocardial insufficiency were present. Laboratory data showed: hemoglobin, 100 per cent; red blood cells, 7,750,000 per cubic millimeter. A right ventricular preponderance was apparent from the electrocardiogram. The patient was discharged in an improved condition after five days in the hospital. He was readmitted because of increasing cardiac failure in September 1928, when the findings were essentially as before. The course was slow but steadily downhill. The signs of mounting venous congestion were again accompanied by a loud systolic murmur, the diastolic murmur having meanwhile become more distinct. Death occurred on April 19, 1929.

The postmortem examination was performed by Dr. Wells twelve hours later. The body was that of a small, slender man, 167 cm. long, weighing 42.9 Kg. There were widespread signs of chronic passive congestion. The heart was greatly enlarged, weighing 870 Gm. Its anterior surface was composed entirely of a very large right atrium and ventricle, the latter forming the apex. The left atrium and ventricle were not increased in size. The tricuspid, pulmonary and mitral orifices were dilated, but they presented, in common with the aortic orifice, no evidences of insufficiency. The leaflets of the mitral valve were slightly thickened as the result of a work hypertrophy but were in no sense stenosed. The foramen ovale was enormous and entirely unprotected, measuring 4 cm. in diameter. Both atria had moderately hypertrophied walls. The myocardium of the right ventricle was tremendously hypertrophied despite great dilatation of the chamber; the wall of the left ventricle was normal. The pulmonary artery was large, measuring 12 cm. in circumference; the aorta was small, measuring 6 cm. The pulmonary veins were enlarged. The ductus arteriosus was obliterated; the coronary arteries appeared essentially normal.

Microscopic examination of the myocardium of the left ventricle showed no fibrosis or Aschoff bodies.

CLINICAL DATA

Our case of defect of the interauricular septum associated with mitral stenosis presents a number of features which deserve comment. Of the twenty-six previously reported cases, twenty-two occurred in females and only four in males. Our patient is the fifth male.

The published reports indicate that the condition is usually fairly well tolerated. Of the twenty-six patients, all save three were adults. Of the three children, one died at 16 years, and one at 13, and one, a new-born child, lived only two and one-half days. This last case, reported by Donnally,[4] was one of the infantile type of coarctation of the aorta, together with developmental mitral stenosis and an incidental open foramen ovale. This is an essentially different pathologic picture,

4. Donnally, H. H.: Congenital Mitral Stenosis: Report of a Case of Developmental Mitral Stenosis Combined with Hypoplasia of the Left Ventricle and Auricle, Rudimentary Aorta and Other Defects, J. A. M. A. **82**:1318 (April 26) 1924.

and it seems doubtful whether the case should be included in the series. Our patient, who died at the age of 10 years, is the youngest described in reported cases of defect of the interauricular septum complicated by acquired mitral stenosis.

In the previously reported group, in only four cases was there a history of rheumatism. In this case there was a frank history of pains in the joints, and a characteristic rheumatic erythema was repeatedly observed.

Physical examination of our patient revealed two other congenital anomalies in addition to the cardiac condition, namely, congenital incomplete coloboma of both eyes and a mild degree of hypospadia. In addition, a Meckel diverticulum was found at autopsy.

The murmur heard over the cardiac area merits consideration. Numerous examiners agreed that the murmur was harsh, systolic in time and maximum over the midprecordium at about the third left interspace. Following the pains in the joints, the bouts of fever and congestive failure suggested the presence of acquired cardiac disease, but at no time were we able definitely to make out a murmur at the apex characteristic of mitral involvement. We felt that the original murmur, which was first heard when he was 19 months old and which persisted with little change until the end, must have been due to the open foramen ovale. Moreover, it is of interest that in the case of uncomplicated open foramen ovale cited as a control case a similar murmur was heard, systolic in time, with maximum intensity in the third left interspace. These findings would seem of some importance, as there is considerable uncertainty among cardiologists about the nature of the murmur which may arise from defect in the interauricular septum.

A final interesting observation was the intense cyanosis present during the last two days of life, a phenomenon so frequently encountered as a terminal event in cases of defect of the interauricular septum.

PATHOLOGY

In our 10 year old subject we found a tremendously enlarged heart. This enlargement was the apparent result of a widely open foramen ovale with an engrafted rheumatic endocarditis and myocarditis, leading to well marked mitral stenosis and insufficiency, mild tricuspid insufficiency, endocardial thickening and myocardial hypertrophy and scarring. The pulmonary artery was large; the aorta, hypoplastic. There was widespread evidence of myocardial failure.

It is of particular interest to find in Dr. Wells' case almost identical anatomic changes in the heart in the complete absence of rheumatic

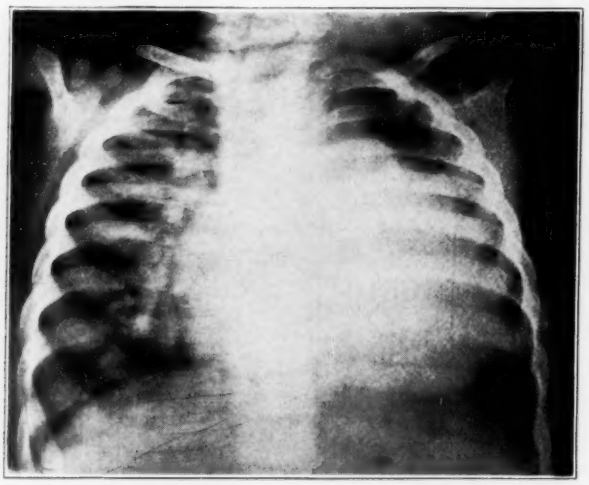

Fig. 4.—Roentgenogram of H. A., aged 19 months, taken on Oct. 31, 1924. The cardiac enlargement, the prominent pulmonic conus and the increased hilar markings are evident.

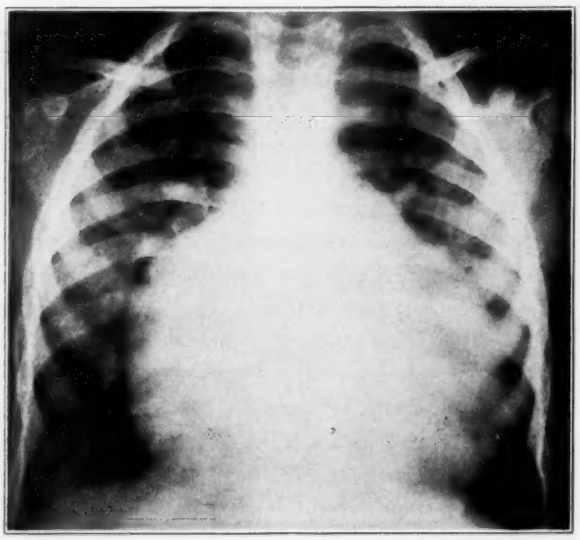

Fig. 5.—Roentgenogram of H. A. at the age of 3 years and 4 months (July 27, 1926). The enlargement on the right side, which is more definite than in figure 4, antedated the appearance of the first rheumatic symptoms.

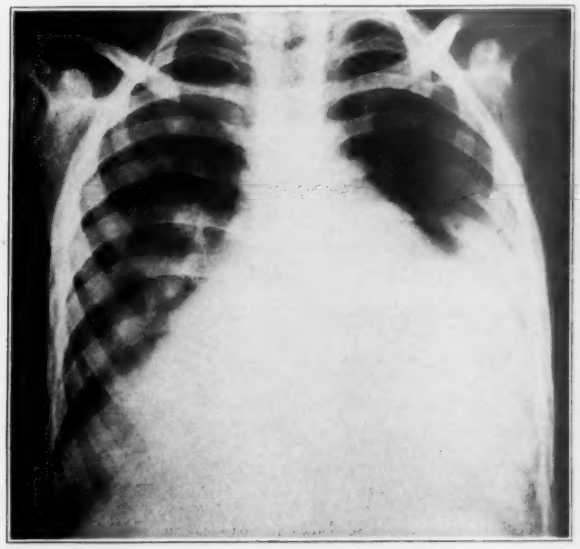

Fig. 6.—Roentgenogram of H. A. at the age of 9 years and 7 months (Nov. 1, 1932). The cardiac outlines are more or less obscured by pulmonary congestion.

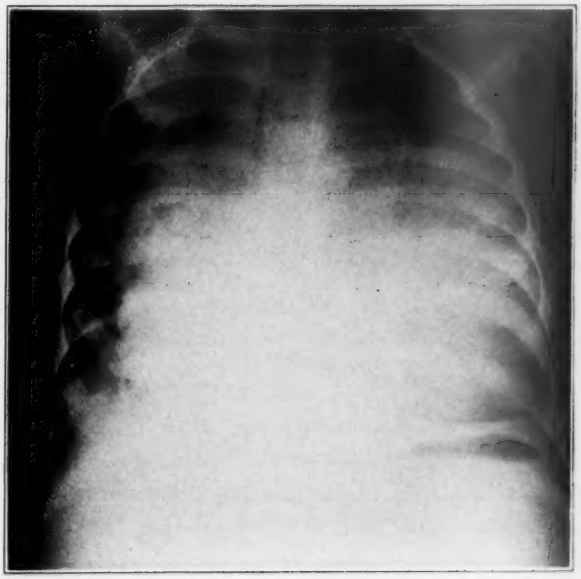

Fig. 7.—Roentgenogram (post mortem) of H. A. at the age of 10 years and 7 months (Nov. 1, 1933), showing the tremendous cardiac enlargement.

infection. In this case the patient showed the same great hypertrophy of the chambers of the right heart and the same large pulmonary artery and small aorta as did our patient. In this instance, however, the only possible cause for these changes and the subsequent myocardial failure lay in the large interatrial communication, mitral stenosis being strikingly absent.

The association of a patent foramen ovale with an enlarged pulmonary artery and small aorta has long been known. In the absence of any evidence of bacterial endocardial infection, the large foramen ovale of

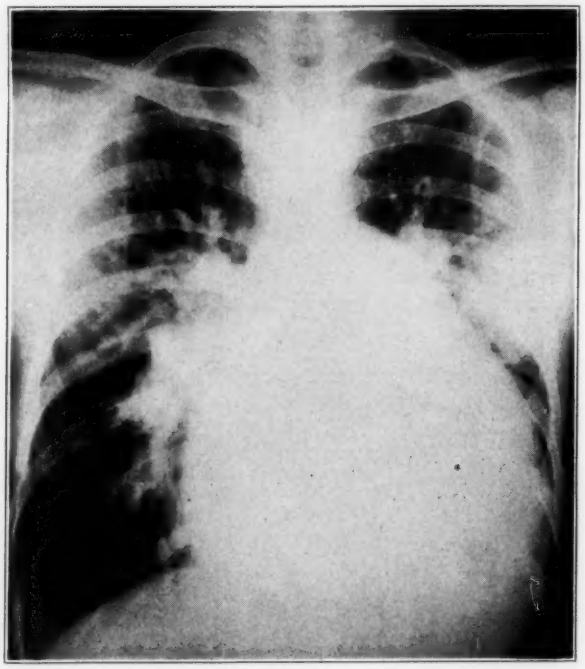

Fig. 8.—Roentgenogram of M. L., aged 26 years, with an uncomplicated widely patent foramen ovale, showing cardiac enlargement, prominent pulmonary conus and hilar shadows and absence of an aortic knob.

our patient must surely be a congenital failure of development of the septum secundum. It seems reasonable to assume that the interatrial defect with attendant flow of blood from the left atrium to the right (fig. 2) causes an increased load for the right chambers and accounts for their customary disproportionate enlargement. The large pulmonary artery may perhaps be explained on a similar basis. To speculate on the possible connection between a true patency of the interatrial septum and rheumatic involvement of the mitral valve appears groundless.

ROENTGENOLOGIC DATA

Dressler and Rösler [5] and McGinn and White [1] stressed the characteristic roentgen picture, which they thought permitted diagnosis ante mortem. The diagnostic features are the narrow aorta, the large pulmonary conus, the wide shadows of the hili of the lungs and the hypertrophy of the right side of the heart.

The roentgenograms of our patient (figs. 4-7) show these features fairly well. The roentgenogram of the patient with defect purely of the interauricular septum (fig. 8) shows beautifully the features cited by McGinn and White as characteristic of the combined lesions.

Because of the similar condition of the chambers of the heart and of the great vessels in the two reported subjects, it is only natural to expect roentgenologic similarity. We cannot, therefore, agree that the roentgenogram is sufficiently distinctive to permit an exact diagnosis during life.

SUMMARY

We have presented the case of a 10 year old boy showing a widely open foramen ovale associated with an acquired mitral stenosis.

We have presented the case of a 27 year old man showing a widely open foramen ovale not associated with mitral stenosis.

The similarity of the physical, pathologic and roentgenologic findings in the two cases has been discussed.

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5. Dressler, W., and Rösler, H.: Vorhofseptumdefekt kombiniert mit Mitralstenose und aurikulärem Leberpuls, Ztschr. f. klin. Med. **112**:421, 1930.

KAPOSI'S VARICELLIFORM ERUPTION

REPORT OF THREE CASES

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As a definite entity occupying a place among accepted cutaneous diseases, Kaposi's varicelliform eruption may not yet have acquired recognition. As a clearcut picture, easily recognizable as a certain complication of infantile eczema, it would seem to deserve a niche among the rarer dermatoses. The instances reported by Brown [1] and McLachlan [2] and accompanied with excellent photographs clearly informed one of us (E. F. C.) as to the nature of two cases which stood out as well recalled but baffling experiences of dispensary work. Perusal of literature dealing with infantile eczema and with other types of suggestively umbilicated outbreaks, together with informal conversations with several well informed dermatologists about the matter, had been productive of no results. Nevertheless the syndrome seemed so clearcut that it was felt that the condition was worthy of description and probably one already set forth in print. The Scotch dermatologists' articles settled the question. In addition to the cases reviewed by Brown and McLachlan a few more instances have recently been reported. Frühwald [3] collected three examples in young adults, all of whom had long-standing eczema or seborrheic dermatitis. The etiology of pustulosis vacciniformis acuta, by which term Juliusberg [4] described the condition, has received consideration by Freund.[5] Guarnieri's corpuscles were reported in sections of the eyeball of a rabbit the cornea of which was inoculated with the contents of a pustule. After recovery the patient was vaccinated without trace of immunity present. Freund's

1. Brown, W. Herbert: Kaposi's Varicelliform Eruption, Brit. J. Dermat. **46**:1 (Jan.) 1934.

2. McLachlan, Allison David: Kaposi's Varicelliform Eruption, Brit. J. Dermat. **46**:8 (Jan.) 1934.

3. Frühwald, R.: Pustulosis vacciniformis acuta beim Erwachsenen, Dermat. Wchnschr. **99**:922 (July 14) 1934.

4. Juliusberg, F.: Ueber Pustulosis acuta varioliformis, Arch. f. Dermat. u. Syph. **45**:21, 1898.

5. Freund, H.: Zur Atiologie der Pustulosis vacciniformis acuta (Kaposi-Juliusberg), Dermat. Wchnschr. **98**:52 (Jan. 13) 1934; abstracted in Wise, Fred, and Sulzberger, M. B.: Year Book of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1934, p. 174.

conclusion was that an attenuated vaccine virus, unable to induce specific immunity, acted conjointly with highly virulent staphylococci. As we have not noted articles on the subject in American literature, we wish to set forth briefly the three instances of Kaposi's varicelliform eruption coming to our notice in order that its incidence in this country may be recorded. The third case was added from the hospital practice of one of us (J. B. L.).

REPORT OF CASES

CASE 1.—A girl 1 year of age was seen in the spring of 1929 at the dermatologic dispensary of the Children's Hospital. She was demonstrated before a small ward class of postgraduate pediatric students. For several months the child had had eczema of the face, for which condition she had been brought to the dispensary on several occasions. A few days prior to the visit in question acute coryza with fever and purulent rhinitis had developed. About the same time the right side of her face became swollen and erupted with reddish spots which rapidly turned to discrete pustules. When examined on the fifth day of the outbreak, the infant's face presented a strictly unilateral outbreak. Umbilicated pustules of quite uniform size, approximately 6 mm. in diameter, were located on an inflamed, markedly swollen base. The right eye was nearly closed by this edema. All lesions appeared to be in the same stage of development. The patient had not been vaccinated for smallpox, nor was there a history of an attack of chickenpox. On the second day following this initial inspection, the appearance had entirely changed from the characteristics just noted. Confluence had taken place; the pustules were almost wholly replaced by yellow crumbly crusts, and the umbilication was practically lost. With the condition treated as pyoderma, progress toward recovery was rapid and satisfactory.

CASE 2.—P. McF., a boy 18 months old, was referred to the dermatologic clinic of the Chestnut Hill Hospital on May 7, 1934, by Dr. F. X. McCarthy of Conshohocken, Pa. Since the age of 3 months the child had had eczema involving the face, hands, wrists and popliteal spaces. For the most part it had been of a dry type, with occasional attacks of oozing. The child had been treated by the family physician with local applications and dietary measures. The patient was somewhat underweight and irritable, but no definite internal pathologic conditions had been observed. A successful vaccination took place when the child was 15 months old. The boy had not had chickenpox, though an epidemic was present in the neighborhood. On April 30 the child was taken acutely ill with fever, running nose and reddened pharynx. Small ulcers were noted on the tongue. The following day an acute eruption was seen to have appeared on the eczematous regions of the hands and wrists. The next morning it had affected one side of the face, the other side breaking out later the same day. Internal medication for the febrile attack had been limited to a laxative and an alkaline mixture. The eruption progressed and, when examined at the time of the first dispensary visit, consisted of uniformly sized, umbilicated, flattened pustules beginning to crust. In number they approximated two hundred, the vast majority located symmetrically on the face. According to the history they did not all erupt simultaneously but were augmented by fresh ones during the first two or three days of the outbreak. When seen, however, they gave the impression of equal age and development. The shoulders, sides of the neck and hands each had a scattered group of from six to ten lesions.

The best description of the individual lesion present was that of a pustule on the seventh day following vaccination for smallpox. Each pustule was quite distinct, though many had coalesced with their neighbors to a certain extent. Each center was marked by a sunken, crusted navel of a dark brown color. At that time the child had a rectal temperature of 102.4 F., a pulse rate of 122 and a respiratory rate of 20 per minute. He was restless and irritable and scratched the facial outbreak unless restrained.

The patient was observed at his home the next day. Overnight the condition had improved markedly. Almost no umbilication was noticeable, crusting having superseded the pustules of the day before. The crusts were of the superficial impetiginous variety, largely coalescent on the face and discrete elsewhere. The temperature had fallen to normal, and the irritability had markedly decreased. A

Fig 1 (case 3).—Lesions on the day after the patient's admission, the sixth day of the disease. Crusting has progressed to a point where many of the umbilications are obliterated. This feature, especially on the forehead, can still be made out with a reading glass.

purulent rhinitis persisted as it had throughout the attack. From that time the outbreak rapidly disappeared and left the eczema much as before. On May 21 at the clinic for allergic conditions the child gave strongly positive cutaneous reactions to egg, milk and wheat. Ten months later the skin showed no evidence of scarring as a result of this outbreak.

CASE 3.—E. R., a white boy aged 9 years, had suffered from eczema since he was 3 months of age. He had contracted varicella during an epidemic in a ward on a previous admission to the Philadelphia General Hospital. He had been in the hospital on ten occasions and spent two years continuously in the institution on one admission. Hospitalization usually improved the condition markedly and relapses followed discharge from such care. The eruption occurred principally on the face

and extremities. The last admission prior to the one in question was on Feb. 13, 1934. He left the hospital on March 21 as usual with a clear skin. Not long after he was discharged the eczema reappeared and treatments at home were instituted with little or no improvement.

Five days before the present admission (Feb. 23, 1935), he was sent home from school complaining of headache. That night he was bathed in a solution of magnesium sulphate, and a dose of the same drug was administered internally. An ointment of unknown composition was rubbed on the eczematous areas in an effort to allay the itching, which was causing him great discomfort. The following morning he was found to be broken out with the type of eruption described in

Fig. 2 (case 3).—Umbilicated pustules superimposed on eczema of upper extremity.

this paper. From that time until admission to the hospital he remained in bed, apparently with fever. He vomited several times and complained of generalized pain and burning of the skin. Physical examination on admission revealed a fairly well developed boy, acutely ill and seemingly in great pain. At times the pain caused him to cry out. He resented being touched anywhere. There was a generalized pustular eruption over the body, superimposed on a scaly erythematous base. The lesions were found mainly on the face, neck, forearms and thighs. Many of the lesions were umbilicated, and they seemed to show a predilection for the extensor surfaces. The outbreak was most marked on the forearms. Only eleven scattered pustules were found on the anterior surface of the trunk, while the back and buttocks were entirely free. The cervical, axillary and inguinal lymph nodes were all enlarged. The sizes ranged from 1 cm. in diameter to the size of a

walnut. The axillary nodes were slightly tender. The scar of a successful vaccination was present on the left part of the upper arm. The white blood cell count was 13,900 per cubic millimeter; the differential count showed polymorphonuclears 32 per cent, lymphocytes 55 per cent, eosinophils 12 per cent and monocytes 17 per cent. On admission the temperature was 103.4, the pulse rate, 110, and the respiratory rate, 27. A later differential count showed 16 per cent eosinophils.

Two days after admission the child suffered a sinking spell of two hours' duration. He became stuporous and for a time responded feebly to stimulating measures. After this attack he improved steadily. The temperature gradually came down to normal by the third day in the hospital. Treatment consisted of applications of 1 per cent aluminum acetate compresses, 2 per cent boric acid ointment and later lime liniment. While insufficient time has elapsed to determine whether the scarring will be permanent, certain areas are sufficiently eroded to justify that impression.

COMMENT

The unilateral distribution of the lesions in the first case naturally caused one to think of herpes zoster, in which condition there is sometimes noted a certain amount of umbilication. Had the eruption been present on both sides, it would have more than suggested variola. Two possibilities were uppermost in consideration. First, multiple inoculation with vaccinia, which the lesions most closely resembled, was rejected because of the lack of contact with any person known to have been recently vaccinated, including the patient herself. This point of view later was confirmed by the absence of typical scarring. Second, it was felt that possibly the discharge from the purulent rhinitis had been smeared across the eczematous surface and had infected numerous foci at one time. Practically, it seemed somewhat incredible that this could be done without contaminating the other cheek also. The fever with the uniform umbilicated outbreak seemed more likely to be a bizarre syndrome connected somehow with the eczematous outbreak.

The condition in the second case was at once recognized as identical with that in the first, save for the bilateral distribution. The same characteristic umbilication of the pustules was most marked. In this instance smallpox was seriously considered, but recollection of the course in the earlier case was reassuring. Besides, the child had been successfully vaccinated three months previously. A profuse purulent nasal discharge was present, but so symmetrical was the outbreak, including the neck, hands and wrists, and so equal in stage of development that it gave evidence more of an internally produced eruption than of a secondary infection from without. The two patients were first seen at about the same stage of development, from the fifth to the sixth day, and consequently the earlier manifestations could be traced only by the histories as given by not too observant mothers. In the case first encountered it seemed useless to culture the drying pustules, as cross-infection had almost surely taken place.

Before admission to the hospital, the last patient (case 3) was seriously regarded as having smallpox until a competent diagnostician from the board of health ruled out that possibility. Afterward, erythema multiforme of the bullous type was the presumptive diagnosis until the patient was seen by the dermatologist in consultation (J. B. L.). The underlying condition of long standing showed a classic appearance of lichenoid eczema (neurodermatitis). Attention is directed to the marked eosinophilia.

The chief value of recognizing this condition is in differentiating it from the "pox" group of exanthems. At times the resemblance may be quite close. The distribution decidedly resembles that of variola as contrasted to that of varicella. In addition, the pox group tends to erupt most abundantly on congested areas, as the site of an inflammatory eruption.

PRIMARY CARCINOMA OF THE PANCREAS IN CHILDREN

REPORT OF A CASE IN A BOY FOURTEEN AND ONE-HALF YEARS OF AGE, WITH GENERALIZED METASTASES

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Oberling and Guérin [1] made a careful review of carcinoma of the pancreas in 1931. They noted that before the discovery of Wirsung's canal tumors and indurations of the pancreas were reported. Later case reports multiplied so that at the end of the eighteenth century "neoplastic injury" of the pancreas was considered very frequent. These authors held that it is obvious that the majority of the cases of "scirrhous pancreas" described at that time were not primary cancers and cited Bayle,[2] who in 1812 was the first to stress the rarity of this condition, and also Claessen,[3] who in 1842, from a study of all cases of cancer of the pancreas published up to that time, showed that under the term "scirrhous" were grouped primary cancers, secondary tumors and chronic pancreatitis. This confusion, owing to the absence of histologic verification, continued throughout the greater part of the nineteenth century.

Other reliably compiled statistics point to the infrequency of cancer of the pancreas and the rarity of this disease during the first two decades of life. Oser's [4] report in 1903 listed 67 cases, the youngest patient being 30 years of age. He cited the study by Biach of 23,611 autopsies, in which were found 2,005 cases of cancer, only 29 of which were in the pancreas. At the Peter Bent Brigham Hospital during a thirty-three year period, Kiefer [5] reported 33 cases, the youngest patient being 33.

Philipp,[6] in his critical compilation of all cases of carcinoma in childhood reported in the literature before 1907, stated that authentic

From the Pediatric Department of St. Vincent's Hospital.

1. Oberling, G., and Guérin, M.: Cancer du pancréas, Paris, Gaston Doin, 1931.

2. Bayle and Coyal, quoted by Oberling and Guérin.[1]

3. Claessen, quoted by Oberling and Guérin.[1]

4. Oser, L., in Nothnagel, C. W. H.: Encyclopedia of Practical Medicine, Philadelphia, W. B. Saunders Company, 1903, vol. 9, p. 148.

5. Kiefer, E. D.: Carcinoma of the Pancreas, Arch. Int. Med. **40**:1 (July) 1927.

6. Philipp, P. W.: Carcinoma Formation in Childhood, Ztschr. f. Krebsforsch. **5**:326, 1907.

primary carcinomas of the pancreas were demonstrated microscopically in only 10 children. It could not be determined which 10 cases he referred to, but probably they are ones which he accepted without recourse to the original articles. This seems to be the case, for later in the same article he stated that of 7 cases of primary carcinoma of the pancreas in children known to him, the following 3 were certain, to wit: the case observed by Bohn,[7] in an infant 6 months old, with involvement of the liver and of the portal and retroperitoneal glands; that reported by Kuehn[8] in a 2 year old girl, with a cylindric cell adenocarcinoma involving the lung and adjacent lymph nodes and with enlargement of the liver, and that described by Simon,[9] in a boy 13 years old, with involvement of the duodenum, liver and kidney. He regarded the case which Bandelier[10] observed in a boy 13 years old as identical with that of Simon, and this seems to be true although they are reported under both names, first by Simon in 1889 and again by Bandelier in 1896.

Philipp did not accept the case described by Rokitansky[11] in a newly born child for lack of descriptive evidence, nor could such a report be found in a survey of the literature, although the case is frequently referred to. He excluded a case reported by Todd,[12] which occurred in a 14 year old girl, for the same reason, and one by Battersby,[13] also in a 14 year old girl, because, as he stated, he did not see the article in the original language. A search of the literature revealed that these two cases are identical, being first reported by Todd in 1818 as an instance of a "remarkable enlargement of the biliary duct" and later referred to by Battersby in 1844. Neither article has a microscopic description. Todd merely described a scirrhous condition of the pancreas and of the surrounding structures closely adherent to the duodenum which he found at operation. Philipp intimated concerning the case observed by Hoff-

7. Bohn, A.: Krebs der Leber, der portalen und retroperitonealen Lymphdrüsen und des Pancreas bei einem halbjährigen Kinde, Jahrb. f. Kinderh. **23**:144, 1885.

8. Kuehn, A.: Ueber primäres Pankreascarcinoma im Kindesalter, Berl. klin. Wchnschr. **24**:494, 1887.

9. Simon, F.: Ueber ein Pankreascarcinoma bei einem 13-jährigen Knaben, Inaug. Dissert., Greifswald, J. Abel, 1889.

10. Bandelier, B. E. G.: Beitrag zur Casuistik der Pankreastumoren, Inaug. Dissert., Greifswald, J. Abel, 1896.

11. von Rokitansky, C.: Handbuch der pathologischen Anatomie, Vienna, Braumüller & Seidel, 1842, vol. 3, p. 397.

12. Todd, C. H.: A Remarkable Enlargement of the Biliary Duct (Which Appeared to Be the Consequence of an Indurated State of the Pancreas), Dublin Hosp. Rep **1**:325, 1818.

13. Battersby, F.: Recherches sur le diagnostic des maladies du pancréas, Gaz. méd., Paris **39**:620, 1844.

man,[14] that of an infant who died one-half hour after birth with necropsy showing icterus of the skin and cancerous infiltration of the liver, pancreas and mesenteric lymph nodes, that the condition probably was not cancer of the pancreas since the mother had had five previous stillbirths without apparent cause. No histologic observations were given.

Luttinger [15] stated that reliable statistics supported by histopathologic observations revealed the following 6 cases of primary carcinoma of the pancreas in children: those of Rokitansky, Bohn, Kuehn, Simon, Bandelier and Dutil.[16] The reference to Dutil's case (1884) seems to be an error, for I was unable to find such an article. In the same periodical, in 1888, Dutil [17] reported a case of primary carcinoma of the head of the pancreas in a man 47 years of age. Philipp did not mention it, and neither he nor Luttinger mentioned the case of Mondière,[18] who in 1836 reported this condition in a boy 12 years of age. Luttinger also made no mention of the case reported by Stewart and Stewart.[19]

Pack and Lefevre,[20] in their statistical data gathered from the records of the Memorial Hospital, New York, during a period of twelve years prior to 1929 and consisting of 19,129 cases of neoplasm, found 16,565 to be malignant; of these 8,007 were in men and 8,558 in women. In their collection, sarcomas comprised 10.4 per cent of all malignant tumors and carcinomas 89.6 per cent, with an average age of 38.2 years for the patients with sarcoma and 53.9 years for those with carcinoma. In this entire series there were only 21 cases of cancer of the pancreas, the youngest patient being in the third decade of life. They reported no tumors of any kind in the gastro-intestinal tract and accessory organs (exclusive of the oral cavity) in children under the age of 15 years. Their study shows that carcinoma of the pancreas is predominant in men, who comprised 71.4 per cent of the 21 patients in this group.

Helmholz [21] made a study of the 750 cases of malignant disease in children aged less than 15 years occurring at the Mayo Clinic in the

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14. Hoffman, quoted by Philipp.[6]

15. Luttinger, P.: Malignant Growths in Children, Cancer **2**:27, 1934.

16. Dutil, A., quoted by Luttinger.[15]

17. Dutil, A.: Note sur un cas de cancer primitif de la tête du pancréas, Gaz. méd., Paris **5**:445, 1888.

18. Mondière, J. T.: Arch. méd. de Paris **2**:56, 1836.

19. Stewart, S. C., and Stewart, L. F.: A Case of Cancer of the Pancreas in a Nine Year Old Boy, with Notes on Other Reported Cases of Cancer in Children, Internat. Clin. **2**:118, 1925.

20. Pack, G. T., and Lefevre, R. G.: The Age and Sex Distribution and Incidence of Neoplastic Diseases at the Memorial Hospital, New York City, J. Cancer Research **14**:167 (June) 1930.

21. Helmholz, H. F.: Malignant Neoplasma in Childhood, Proc. Internat. Assemb. Inter-State Post-Grad. M. A., North America, October 1931, p. 209.

ten year period from 1921 to 1930 inclusive. There were only 5 cases, or 0.66 per cent, of tumors in the gastro-intestinal tract, and these were all sarcomatous. He pointed out that the distribution of tumors in childhood and in adult life differs widely and that even more marked was the difference in incidence of sarcoma and carcinoma in the same period. He agreed with others that all but 3 per cent of tumors in childhood are sarcomas, while practically 90 per cent in adults are carcinomas.

Stout [22] stated that during a ten year period at the Presbyterian Hospital, New York, only 33 cases of primary carcinoma of the pancreas were recognized among 1,862 of cancer of all kinds, a percentage of 1.77. Neither sex showed a preponderance, and, as in most cases of carcinoma, the disease occurred distinctly in the later years of life; 76 per cent of the patients studied had passed the fifth decade of life, and there were no children.

Leven,[23] in a study of 14,739 autopsies from various sources, observed only 99 cases of cancer of the pancreas, the youngest patient being 38 years of age.

Stewart and Stewart [19] in 1915 reported a case of cancer of the medulla of the pancreas in a 9 year old boy. These authors accepted the cases reported by Kuehn and Simon as the only proved cases of pancreatic cancer they were able to find in the literature. They rejected the cases observed by Rokitansky and Todd but made no mention of the case reported by Bohn, which seems well substantiated by the observations at necropsy. In their own case an exploratory operation revealed a nodular tumor of the tail of the pancreas, and the entire organ was slightly enlarged, hard and irregular but freely movable. A few reddish lymph nodes were noticed along the upper and lower borders of the tail. No other tissues were observed to be involved. Twelve days later the child died. An incisional autopsy was the only available procedure, and this showed the pancreas to be about twice as large as it was at the time of operation and of the same appearance. Microscopic examination showed a network of fibrous tissue that was quite thick in areas and occupied by islands of endothelial-like cells, closely packed. Some of these cells showed mitotic figures, and some of the islands of cells were generally necrotic; others showed central necrosis with signs of phagocytic action. Some were isolated; others were clumped and separated by thin projections of fibrous tissue. In concluding, these authors stated that there was no evidence suggesting that the cancer was not primary in the pancreas, nor was there evidence of cancer elsewhere.

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22. Stout, A. P.: Human Cancer, Philadelphia, Lea & Febiger, 1932, p. 167.

23. Leven, N. L.: Primary Carcinoma of the Pancreas, Am. J. Cancer **18:** 852 (Aug.) 1933.

Stout and Todd,[24] in 1932, reported a case of primary adenocarcinoma of the pancreas in a 4 year old child. In their case the only part of the pancreas involved was the head and 1 cm. of the body, by a tumor 2 cm. in diameter. The liver was involved, but the gallbladder was normal. Lymph nodes near the pancreas and along the vertebral column up to and including those of the celiac group were involved. No mention of other metastases was made. The authors found the tumor to have highly malignant characteristics of the duct cell type and observed that neoplasms of this nature may arise in either the liver or the pancreas. They stated that the finding of a solitary nodule in the pancreas, with multiple nodules in the liver, was a significant and a logical sequel of events and quoted Ewing [25] (1928) as stating that metastases commonly occur in carcinoma of the pancreas and appear first in the adjacent lymph nodes and then in the liver. In addition, in support of their contention that the cancer was primary in the pancreas, they showed the histologic arrangement of the cancer cells and cytologic resemblance between them and the normal ductal tissue.

REPORT OF CASE

History.—A white boy, aged 14 years, 7 months and 19 days, was admitted to St. Vincent's Hospital on April 17, 1933, complaining of extreme weakness, cough, pain in the right side of the chest and loss of appetite and weight. He was born in New York of Irish parents, who were living and well. There were two other children in the family, both of whom were said to be in good health. There had been no other pregnancies. There was no family history of malignant disease, diabetes or tuberculosis, nor was there any history of exposure to tuberculosis. In early childhood the patient had measles and mumps. At the age of 9 years he was operated on at another hospital for an acute attack of appendicitis, after which operation draining continued for six weeks, but he made a good recovery. With these exceptions he had had no previous illness and no accidents or injuries of any importance.

About five months prior to admission to the hospital the patient became weak, was easily fatigued and began to lose weight. All of these symptoms progressed gradually; appetite began to fail, and shortly there was dyspnea on even slight exertion. At the end of the first week of illness the boy complained of a dull, nonradiating pain in the lumbosacral region, which persisted for about a week. A week later a severe dry cough developed, and the child complained of pain in the lower part of the chest on the right side, which was made worse by coughing and deep breathing. At times this pain was severe, and it persisted for about one week. Then he felt a pain in the posterior region of the left thigh, which was not severe and lasted but a short time. The cough persisted, with mucopurulent sputum, which contained neither blood nor tubercle bacilli. Two days before admission he had a severe nosebleed and vomited about one-half cupful of clotted blood.

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24. Stout, B. F., and Todd, D. A.: Report of a Case of Primary Adenocarcinoma of the Pancreas in a Four Year Old Child, Texas State J. Med. **28:** 464 (Nov.) 1932.

25. Ewing, James: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928.

It was said that his stools had been black for about three weeks, during which time he had been taking a "blood tonic." It was thought that he had lost more weight in the three weeks prior to admission to the hospital than in the previous four months.

Physical Examination.—The patient was a tall white boy, emaciated, weak and pale but without icterus. He was well oriented and cooperative. Marked dental caries was present. The superficial lymph nodes of the neck were slightly enlarged on both sides; the largest one, in the left anterior cervical chain, was about as large as an almond. All were firm, movable and not tender. The chest was symmetrical, but there was only slight respiratory excursion. There was a short systolic murmur in the region of the apex of the heart; the rate was 110 and the rhythm regular. There was marked dulness at the base of each lung, and the percussion note was slightly high-pitched, somewhat more so on the right side. Fine râles were heard over these areas only on coughing. The breath sounds were loud and harsh throughout. The heart did not seem to be displaced. There was an old scar in the right lower quadrant of the abdomen. There was no spasm or rigidity. The abdomen was well rounded and moderately resistant, especially in its upper half, where a mass of considerable size was palpated. The mass occupied a considerable part of the right side of the abdomen, extending downward almost to the umbilicus and well into the region of the left hypochondrium. The surface and edge of this mass were definitely nodular. The spleen was not felt. No tenderness was elicited.

Course.—The course during the time in the hospital was one of rapid decline to a fatal end. Prostration became more profound, and the cough increased in severity and became more productive, being distressing at times but not causing any pain. The patient was given blood transfusions twice without any immediate or remotely apparent benefit. He had an occasional nosebleed. The temperature varied from slightly subnormal to 100.6 F. No petechiae had been seen. The nodular surface of the tumor became more marked. The mass itself became more extensive and extended downward to the umbilicus and almost to the right of the crest of the ilium. The respiratory rate remained throughout about 30 per minute. The pulse rate fluctuated between 110 and 140, only occasionally being as low as 90. There were no gastro-intestinal symptoms except during the last six hours, when he became incontinent of feces, during which time he was also incontinent of urine. After sixteen days in the hospital, the boy died on May 3, 1933.

Laboratory Findings.—The erythrocytes numbered 1,420,000 and the leukocytes 13,200 per cubic millimeter of blood; the hemoglobin content was 5.4 Gm. per hundred cubic centimeters of blood (32 per cent). The differential count showed: polymorphonuclears, 80 per cent; lymphocytes, 20 per cent, and eosinophils, 2 per cent. There were marked achromia, anisocytosis, poikilocytosis and many red cells of the regenerative type. The sedimentation rate was normal. Urinalyses revealed the presence of a moderate amount of bile, from few to many pus cells, a small amount of albumin and an occasional hyaline and granular cast, but never red blood cells. The feces showed marked reaction to guaiac. The Wassermann test of the blood and repeated Mantoux tests (amount of tuberculin increased to 5 mg.) gave negative results, and the sputum did not contain tubercle bacilli. Chemical examination of the blood showed: sugar, 143 mg.; nonprotein nitrogen, 39 mg., and chlorides, 495 mg., per hundred cubic centimeters. Two days later the results were: sugar, 107 mg.; nonprotein nitrogen, 30.7 mg., and chlorides, 478 mg., per hundred cubic centimeters. The icteric index was 4.2, and the van den Bergh test showed: immediate direct reaction, negative; delayed direct reaction, positive.

A roentgenogram of the chest revealed a marked enlargement of the hilar shadow on the right, and the supracardiac shadow on the right showed a definite widening in its lower portion. The left hilar shadow was also enlarged and sharply circumscribed. Both pulmonary fields showed innumerable small rounded shadows of increased density, which occupied all portions of the lungs with the exception of the apexes. The practically complete absence of involvement of the apexes is noteworthy.

A flat plate of the abdomen revealed nothing remarkable. Roentgenograms of the cranial vault and of both upper and lower extremities showed nothing abnormal. The urinary tract after injection of skiodan showed that the right kidney occupied a vertical axis and was displaced moderately toward the right spinal border.

Necropsy.—The postmortem examination was performed about ten hours after death by Dr. A. Fraser, pathologist at St. Vincent's Hospital, from whom I obtained a report of the examination.

The meninges showed considerable serous edema. Both lateral ventricles contained the normal amount of fluid, which was tinged with blood. The rest of the brain was entirely normal.

The pleural cavities contained no fluid. The mediastinum was markedly widened by the presence of several large peritracheal and peribronchial lymph nodes, some of which were the size of a hen's egg. On section these lymph nodes showed mostly necrotic tissue resembling caseous degeneration. Small pieces of firm white tissue resembling malignant metastases were found in these lymph nodes.

The thymus was small and showed two or three nodules of tissue which resembled the tumor tissue found elsewhere.

The lungs were large and firm and maintained their shape perfectly when placed on the dissecting board. The surfaces were shaggy and showed a fine pattern of lymphatic structures. A large part of both lungs showed fine mottling and the same pattern that was noted on the pleural surfaces. Throughout both lungs there were numerous pea-sized nodular lesions, white and raised from the cut surfaces.

The heart was normal.

The peritoneal cavity contained from 300 to 400 cc. of yellow turbid fluid.

The liver (fig. 1) was very large and studded throughout with numerous raised masses, ranging from the size of a pea to the size of a half-dollar. The nodules were yellowish white, some showing hemorrhagic surfaces, and each nodule was surrounded by a circular hemorrhagic area about 1 mm. wide. The cut surface of the liver showed these nodules to contain neoplastic tissue. At the base of the liver the perigastric lymph nodes, the periaortic lymph nodes, the pancreas and the mesenteric lymph nodes were involved in almost one solid mass, which extended across the abdomen from one suprarenal gland to the other.

On section the pancreas showed tumor tissue involving a large part of the organ from the head to the tail.

Enlarged periaortic lymph nodes extended downward to the pelvis; one was the size of a hen's egg and deep purple; on section it was composed largely of necrotic tissue and hemorrhage. All of these lymph nodes showed neoplastic tissue.

The kidneys were large and pale. The right kidney showed a moderate degree of hydronephrosis due to obstruction of the right ureter by involvement in the metastatic mass. Sections showed both kidneys to be very pale, with marked striations of the pyramids. At the upper pole of both kidneys, in the region of the adrenals, the cortex was very yellow.

Both adrenals were large and involved in the tumor mass. On section they both showed neoplastic tissue replacing the medulla in places, more neoplasm being present in the right than in the left.

The spleen was large and purple, and section showed congestion and marked prominence of the malpighian corpuscles.

The stomach and intestines did not appear to be involved.

The gallbladder (fig. 1) was slightly distended but did not appear to be involved by metastases, and the common bile duct was patent to the duodenum.

Fig. 1.—Liver (about one-seventh actual size). The surfaces are covered with numerous nodules, carcinomatous metastases.

Microscopic examination of sections taken from the pancreas (fig. 2) revealed areas completely replaced by carcinoma cells showing alveolar arrangement. In these areas there were replacement of acinar and islet tissues and disappearance of the intra-acinar and interacinar ducts. When the carcinomatous invasion was not so marked, there were hypertrophy and hyperplasia of the islands. Areas were present in which no carcinoma cells could be found but which showed hyperplasia of both the islet and the acinar cells. The carcinomatous cells resembled to a certain extent those of the normal acinar tissue but showed anaplastic changes. There were places in which the transition from the normal cell to the neoplastic cell was clearly seen.

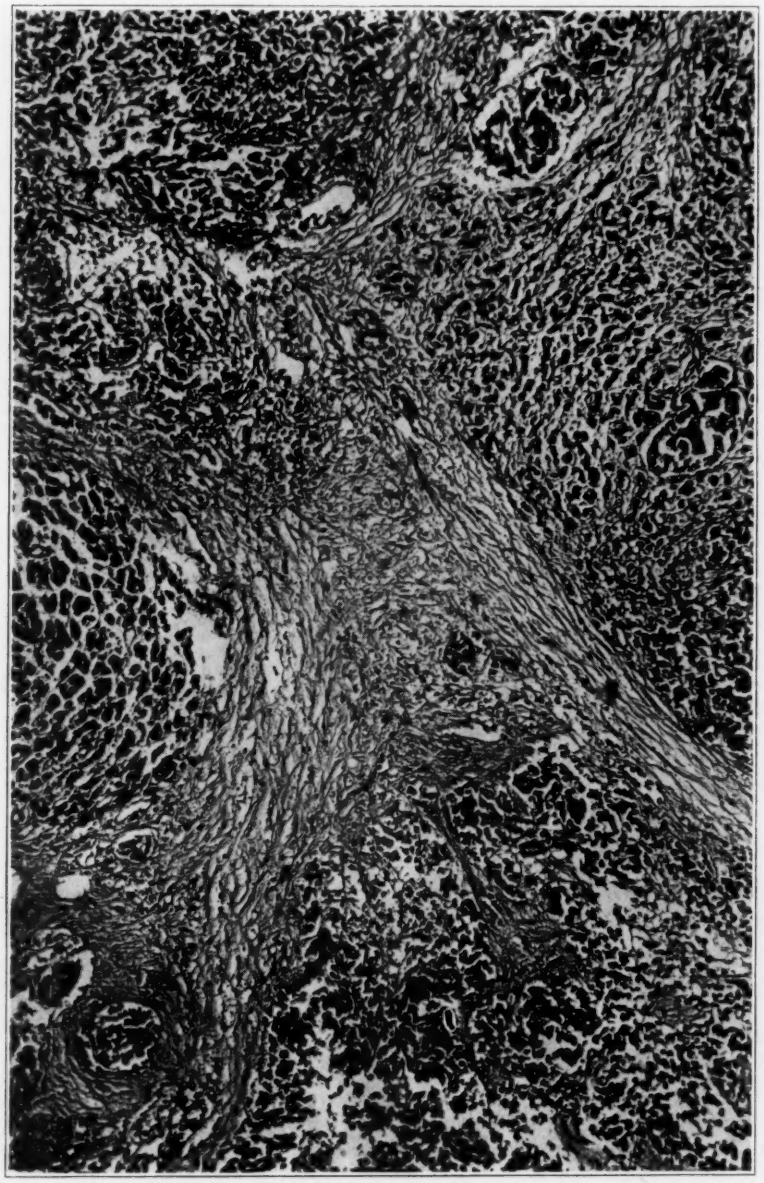

Fig. 2.—Photomicrograph of a section showing hypertrophy of the pancreas with normal island, upper right, and extensive replacement of pancreatic acini by carcinoma cells, lower right and upper left.

Sections taken from nodules in the liver showed complete replacement of the liver cells with closely packed carcinoma cells, exhibiting numerous mitotic changes and alveolar arrangement. Bordering the nodules, the sinusoids of the liver were infiltrated with carcinomatous cells, distending the sinusoids and flattening the liver cells. The areas surrounding the nodules showed the presence of many red and white blood cells, with distention of the biliary capillaries by blood pigments.

The lymphatic glands of the lungs showed solid infiltration with carcinoma cells. Some of the carcinomatous masses were large and showed areas of central necrosis.

Many areas of pulmonary edema and hemorrhage in the alveoli were present. Carcinoma cells were present in the alveolar lining and were found lying free in the alveolar spaces.

Sections from the mesenteric lymph nodes revealed nodular carcinomatous masses, several of which were almost completely necrotic and hemorrhagic. Many other lymph nodes showed almost complete carcinomatous replacement of lymphoid tissue, while many others presented an alveolar structure closely resembling the pathologic structure found in the pancreas.

Sections from both adrenals showed alveolar carcinoma, more marked in the medulla, which was almost entirely replaced. Some areas of the cortex showed normal adrenal columns; others were entirely replaced by carcinoma cells extending to the periphery, and still other areas showed infiltration between the columns.

Sections of the thymus showed no definite involvement of the thymic tissue itself, but the adipose tissue surrounding the gland showed many loosely arranged carcinoma cells.

Sections taken from the cardiac end of the stomach showed solid carcinomatous masses in the lymphatic glands of the muscularis. The submucosa and the mucosa showed scattered carcinoma cells extending between the crypts and villi of the mucosa. There was an area of marked carcinomatous replacement in the mucosa near the surface, with a necrotic and ulcerated area of the mucosal surface itself.

Sections of the spleen showed no carcinoma cells. There were marked atrophy of the malpighian corpuscles and distention of the sinuses with degenerated red blood cells and blood pigment.

Sections of the heart muscle showed no pathologic conditions in the muscle cells, but carcinoma cells were found lying freely in the lymphatic glands.

Sections of the kidney showed normal glomeruli. There were some degeneration and destruction of the epithelium of the convoluted tubules, with the presence of casts in the tubules.

The anatomic diagnoses were: diffuse, solid and alveolar adenocarcinoma of the pancreas, with metastases in the lungs, liver, stomach, adrenals and peritracheal, peribronchial, periaortic and mesenteric lymph nodes; hydronephrosis of the right kidney; secondary anemia.

COMMENT

In commenting on the conditions under which cancer of the pancreas is found, Ewing [25] stated that in many cases the growth occurs in the cirrhotic pancreas. He drew a parallel between the liver and the pancreas in this regard, citing Hulst, who observed that carcinoma of

the ducts follows periductal fibrosis, carcinoma of the parenchyma appearing after interstitial fibrosis. From analogy with the liver Ewing reasoned that carcinoma of the pancreatic parenchyma may be regarded as beginning in a functional hyperplasia following cirrhosis, and carcinoma of the ducts, from chronic irritation and stasis in these canals. Many agree that the aging process affects the pancreas anatomically and functionally and that it becomes fibrotic and shrunken, the condition resembling the inadequacy of pancreatic function in cases of so-called benign glycosuria in aged persons (Pack and Lefevre [20]). Since chronic disturbances of this kind are far more common in adults and increase in incidence with advancing years, it is not surprising that cancer of this organ should be rare in childhood. Ewing [25] mentioned the presence of aberrant pancreatic tissue in the duodenal mucosa and about the head of the pancreas, in some of which accessory glands there is extensive multiplication of ducts from which a cylindric cell tumor may arise.

Ewing [25] found that the location of the tumor is usually in the head or extending diffusely over most of the organ and that the growth is much less commonly limited to the body, rarely affecting the tail. Small tumors may be limited to the pancreas, while more advanced growths early infiltrate the surrounding tissues and cause compressions, sometimes occluding the common duct, producing secondary stasis of bile and dilatation of the gallbladder and also producing varicosities of the bile ducts, both extrahepatic and intrahepatic.

In the case reported here, the entire pancreas was invaded, and the adjacent lymph nodes, markedly infiltrated, were fused to the pancreas, presenting an irregular lumping of its surface. The invasion included also the hepatoduodenal chain, forming a large group of nodes at the hepatic hilus and even involving the cardiac end of the stomach. The characteristic syndrome of Bard and Pic [26] was not present. This syndrome consists of progressive jaundice without remissions, great distention of the gallbladder, absence of hepatic enlargement, subnormal temperature and rapid emaciation and cachexia. Ewing pointed out that such clinical features are observed in a majority of cases in which the head of the pancreas is involved. He mentioned the 113 cases reported by Miraillie,[27] in one fourth of which tumors were detected. He cited Miraillie and Eloesser [28] to show that the liver may be considerably enlarged, and Oser, to show that metastases may be bulky. Also, he stated that when the growth involves only body and cauda the ampulla of Vater may remain pervious, the gallbladder is not distended and

26. Bard, L., and Pic, A.: Contribution à l'étude clinique et anatomo-pathologique du cancer primitif de pancréas, Rev. de méd., Paris **8**:257, 1888.

27. Miraillie, quoted by Ewing.[25]

28. Miraillie and Eloesser, quoted by Ewing.[25]

jaundice does not occur. Ewing referred to such clinically atypical cases as those described by Pic and Tolat.[29] In Leven's [28] 99 collected cases he found the liver to be enlarged in 81 per cent and jaundice absent in 5 per cent.

Remarkable features in this case, considering the widespread destruction of the liver and pancreas, are the absence of jaundice, the absence of apparent impairment in the function of the liver and the failure to find any abnormality in the blood on chemical examination. The gall-bladder was, however, slightly distended but not involved in the mass, and the common bile duct was patent to the duodenum.

The loss of pancreatic fluid and bile leads to acholic and fatty stools, but this condition is by no means constant, having occurred in only 20 cases collected by Miraillie,[27] Oser [30] and Fitz.[31] This feature was not present (clinically) in my case. Glycosuria is rare (Ewing), and in 30 cases of primary carcinoma Pearce [32] found intermittent glycosuria in one and diabetes in another, while persistent glycosuria occurred in 21 cases collected by Miraillie and Oser.[33] In the present case repeated urinalyses and tests for blood sugar gave normal results.

Nearly all authors agree that general metastases are not common, probably because the disease is so rapidly fatal. Stout [22] found no metastases in 55 per cent of his patients who came to autopsy. In 33 per cent metastases were limited to the regional lymph nodes and to the liver, and in only 12 per cent were there distant generalized metastases. Narbeshuber [34] found that cancer in the body of the pancreas is much more apt to metastasize to the liver than that in the head, which has a tendency to involve the peritoneum and the mesentery.

It may not be entirely apart from the purpose of this paper to record a few interesting observations made by Pack and Lefevre [20] in their study of a large number of autopsies (19,129) in a hospital especially given over to the study and treatment of cancer. Their study shows the frequency of malignant tumors in the early epochs, as follows: 1. In infancy (from birth to 10 months) "Wilms' tumor or the adenomyosarcoma of the kidney is of frequent occurrence, together with ocular glioma." 2. In childhood "glioma of the eye is the most significant malignant tumor of this period, although Wilms' tumor is frequently found." 3. In the presexual period "there are relatively fewer malignant tumors at this age than at any other time in life." 4. In the pubertal period (from puberty to end of growth) "the tumors of especial

29. Pic and Tolat, quoted by Ewing.[25]
30. Oser, quoted by Ewing.[25]
31. Fitz, quoted by Ewing.[25]
32. Pearce, quoted by Ewing.[25]
33. Miraillie and Oser, quoted by Ewing.[25]
34. Narbeshuber, quoted by Stout.[22]

frequency are the endothelial myelomas, thymomas, gliosarcomas and sarcomas of the testis. Many authors include bone sarcomas (of the long bones particularly) in this bracket, but, as we have previously shown, the relative age incidence corrected on the basis of the proportionate number of the general population living during this period, does not indicate that individuals of this age are preeminently prone to develop bone sarcomas." In the summary, the authors stated: "The five most common malignant tumors in infants and children were Wilms' adenomyosarcoma of the kidney, ocular glioma, teratoma testis, endothelial myeloma and thymoma."

SUMMARY

A survey of the literature reveals the rarity of primary carcinoma of the pancreas in childhood.

A case is reported in a boy aged 14½ years, with metastases in the liver, lungs, stomach and adrenals and in the peritracheal, peribronchial, periaortic and mesenteric lymph nodes.

SUCCESSFUL TREATMENT OF NOMA WITH FORMALDEHYDE

SIM I. McMILLEN, M.D.
KAMAKWIE, WEST AFRICA

Authorities agree that the mortality from gangrenous stomatitis (noma) is extremely high—90 per cent and above. The treatments suggested consist of application of fuming nitric acid, actual cautery or wide excision without any consideration of the future cosmetic effect. The following two cases are reported because in one case the result was remarkable after the application of undiluted solution of formaldehyde (British Pharmacopeia).

REPORT OF CASES

CASE 1.—A native of Sierra Leone, a boy about 15 months old, was admitted to the hospital with swelling of the left cheek and a black circle several millimeters in diameter near the angle of the mouth. Examination of the inside of the mouth revealed a large foul-smelling ulcer filled with débris from tissue. Many of the teeth above and below on the left side were loose because the process had invaded the gums and periosteum. With the child under ether anesthesia the loose teeth were removed, the involved areas were scraped with a Volkmann spoon, and fuming nitric acid was applied. The corner of the mouth containing the black necrotic spot was excised. After operation the mouth was frequently cleansed with antiseptic solutions.

Three days after operation a black necrotic area on the left cheek indicated the extension of the process. Internal examination of the mouth revealed a condition similar to that on admission. Because of the small crowded quarters (three patients were then being housed in the operating room), the patient was discharged. The gangrenous area in the mouth spread, and three days after discharge he died.

CASE 2.—A native girl about 3 years old was admitted to the hospital on the evening of April 15, 1933. The picture was a replica of that in case 1: swelling of the left cheek with a black circular area near the angle of the mouth and a foul ulcer on the inside, which had extended to the gums and periosteum of the adjacent teeth above and below. The child was subjected to the same treatment as the first. At the end of three days the infection was again in full bloom; a fresh black area was noted on the cheek, and the left eye was nearly obscured by the swelling of the cheek.

At this juncture it seemed that any experiment, however rash, might be tried. The ulcer of the cheek and alveolar process was dried with cotton, and undiluted solution of formaldehyde was applied once a day for five days. No other antiseptic was used. No specific remedy could have given better results. After two applications the fetor was gone, and the swelling of the cheek had greatly subsided. After five applications the condition of the mouth was so favorable that the treatment with formaldehyde was discontinued. I felt that the child was now out of

From the Kamakwie Mission Hospital, Kamakwie, Sierra Leone, West Africa.

danger. Then I used hydrogen dioxide in the morning and applied mercurochrome to the mouth at night.

The hard, dry coagulum produced by the formaldehyde fell off, and the child made a rapid recovery. She was discharged on May 9. A circular opening about 1 cm. in diameter was the only deformity present on the cheek.

COMMENT

Rapid extension, stench, destruction of tissues and occurrence in debilitated subjects are characteristics possessed by both noma and tropical ulcer. The etiology of both conditions is unknown. However, tropical ulcer is not confined to children. It is found nearly always on the legs and feet and only occasionally elsewhere on the body. For the treatment of tropical ulcer formaldehyde has proved to be the best remedy. In the past three years I have used it in over one hundred cases with excellent results. It should be applied about three times to the ulcer without any scraping.

Because of the similarities already mentioned between noma and tropical ulcer, I was led to try formaldehyde for noma in case 2. However, it would seem to be wise to substitute formaldehyde for nitric acid at the time of operation. Perhaps scraping is not needed at all. Two or three further applications of formaldehyde might suffice.

SUMMARY

Applications of undiluted solution of formaldehyde (British Pharmacopeia) gave striking results in one case of gangrenous stomatitis after the standard methods failed. Since the present methods of treatment are discouraging, formaldehyde should be given further trial.

Kamakwie Mission Hospital.

STREPTOCOCCIC MENINGITIS

REPORT OF TWO CASES WITH RECOVERY

MENDEL ZELIGS, M.D.
CINCINNATI

Recovery from streptococcic meningitis rarely occurs. Kolmer [1] stated that the mortality is almost 100 per cent. In a series of thirty-three cases from the University of Michigan Hospital,[2] there was only one recovery.

During the past fourteen years there have been fifty-seven verified cases of streptococcic meningitis in the wards of the Cincinnati General Hospital. The probable etiologic factors in this series are found in the table.

Etiologic Factors in Fifty-Seven Cases of Streptococcic Meningitis

Cause	Number of Cases	Percentage of Cases
Otitis media and mastoiditis	17	30
Injuries to the head; operations on ethmoid bone and on the spine	14	24
Cause unknown	11	19
Acute infections of the respiratory tract	6	10
Septicemia of unknown origin	3	5
Ethmoiditis	1	2
Furunculosis	1	2
Nephritis	1	2
Osteomyelitis	1	2
Suppurative cervical adenitis	1	2
Varicella	1	2
Total	57	100

Treatment in these cases consisted chiefly in draining the source of infection when this was possible, repeated lumbar punctures and the injection of antistreptococcus serum intravenously and in some cases intraspinally. In two instances a rubber catheter was sutured into the cisterna magna to provide permanent drainage. Only one of the patients in this series recovered (case 1).

From the Department of Pediatrics of the University of Cincinnati College of Medicine, and the Pediatric Service of the Jewish Hospital.

1. Kolmer, J. A.: Pneumococcus and Streptococcus Meningitis, J. A. M. A. **92**:874 (March 16) 1929.

2. Canfield, N.: Streptococcus Meningitis: Report of a Case with Recovery, J. Michigan M. Soc. **32**:108 (Feb.) 1933.

REPORT OF CASES

CASE 1.—A white girl 6 years of age was admitted to the Cincinnati General Hospital on Aug. 14, 1926, immediately after being struck by an automobile. A hematoma was present over the right supra-orbital region. The right eye was ecchymotic. A small laceration was present over the occipital region. There was a profuse thin bloody discharge from the nose, which had the characteristics of spinal fluid. The biceps reflexes were equal and active. Ankle clonus and the Babinski sign were absent. The temperature was 98 F., the pulse rate 104 and the respiratory rate 20. The following morning, the temperature rose to 101.6 F., and several generalized convulsions occurred. A lumbar puncture revealed cloudy fluid under normal pressure, a culture of which demonstrated streptococci. That afternoon the temperature rose to 105.6 F., and the following morning it dropped to 104 F.

Treatment consisted of daily lumbar punctures and daily injections of 10 cc. of antistreptococcus serum intravenously.

Drainage of spinal fluid from the nose, which was profuse at first, gradually diminished and ceased after about ten days. The temperature remained between 101 and 102 F. for about two weeks and then gradually dropped to normal. The leukocyte count on August 18 (four days after admission) was 21,000 per cubic millimeter, and on September 3 (sixteen days after admission) it was 7,100. The patient was discharged on September 9 (twenty-two days after admission) in good condition, with no residual symptoms.

The spontaneous drainage of spinal fluid through the nose, caused by the basal fracture of the skull, possibly was an important factor in the recovery of this patient.

Only fifty-eight instances of recovery from streptococcic meningitis were found in the literature by Felsen and Osofsky,[3] including one case of their own. In nearly 80 per cent of these cases the meningitis followed either mastoiditis or injuries to the head. Treatment of the patients who recovered varied greatly. In some cases lumbar punctures constituted the only treatment, with the exception of symptomatic therapy. In one instance surgical drainage of the cisterna magna was instituted by the insertion of a drain. In other cases injections of antistreptococcus serum were given intraspinally, intravenously and intramuscularly. In a number of instances the spinal canal was irrigated with saline solution, acriflavine hydrochloride, mercurochrome, gentian violet and other dyes. After extensive experimentation on dogs and trial in some cases on human beings, Kolmer stated the belief that chemotherapy and biologic therapy given intravenously or intraspinally are both useless in cases of streptococcic meningitis. Encouraging results, however, were obtained by the use of dyes and serums injected directly into the carotid arteries. Following Kolmer's work, Crawford[4] injected Pregl's solution directly

3. Felsen, J., and Osofsky, A. G.: Streptococcus (Viridans) Meningitis with Recovery, J. A. M. A. **102**:2170 (June 30) 1934.

4. Crawford, A. S.: The Intracarotid Treatment of Meningitis, J. A. M. A. **98**:1531 (April 30) 1932.

into the carotid arteries, and one of his patients recovered. He recorded another case, observed by Dowman, in which similar treatment was given and recovery followed.

The next case is of interest because injections of air were used to break up an intraspinal block and to facilitate drainage.

CASE 2.—A white boy 11 years of age was admitted to the pediatric service of the Jewish Hospital on Jan. 16, 1935, with the chief complaint of convulsions. The afternoon before admission the patient returned from school complaining of pain in the back of his neck and head. That evening he became nauseated and vomited. Drowsiness followed, and the pains increased in severity. During the night there were three generalized convulsions.

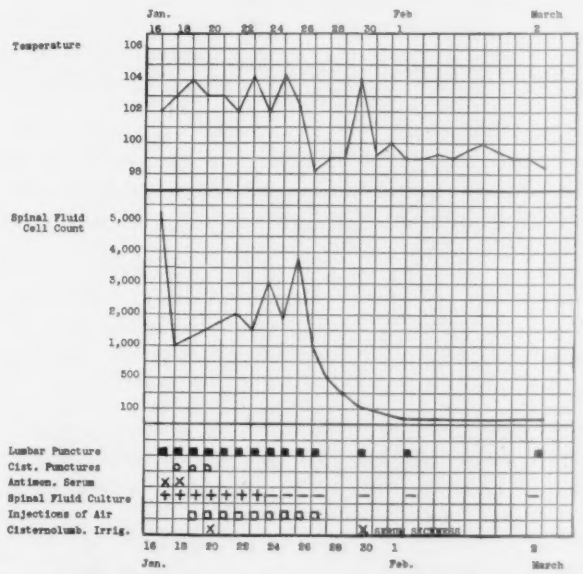

Chart showing the curves for temperature and spinal fluid cell count and the results of the laboratory examinations during treatment.

The past history was interesting, since it would appear that the patient had a cerebral hemorrhage at birth, with resultant mild hydrocephalus and spastic paralysis of the left arm and leg. There had been cyanosis since birth and frequent attacks of dizziness, dyspnea and fainting. The patient did not walk or talk until he was 6 years of age. He had a severe attack of scarlet fever, complicated by otitis media, at the age of 7 years. He had had several attacks of tonsillitis. There had been no previous convulsions. At the age of 9 years the patient had acute osteomyelitis of the left tibia and staphylococcic septicemia, from which he recovered in about two months.

Physical examination on admission to the hospital showed that the patient was poorly developed and undernourished. He was in a semicomatose condition. The respiratory rate was rapid. There was marked cyanosis of the lips, nail beds and skin. The pulse rate was 120 and the temperature 102 F. The neck was

markedly retracted and stiff, and the legs were drawn up in flexion. The head measured 25 inches (63.5 cm.) in circumference. The pupils were contracted and did not react to light or in accommodation. There was no nystagmus or strabismus. No nasal discharge was present. The mouth was firmly closed, and an attempt to open it caused vomiting. The Kernig and the Brudzinski sign were present. There was marked bulging of the precordium. A loud blowing systolic murmur was heard over the entire precordium but best at the pulmonic area. The pulmonic second sound was accentuated and louder than the aortic second sound. A systolic thrill was present. The systolic blood pressure was 90 and the diastolic 60. The lungs on physical examination appeared normal. Examination revealed the abdomen to be normal except that the edge of the liver was palpable at the level of the umbilicus. There was a spastic paralysis of the left arm and leg. A healed operative scar was seen over the left tibia. There was marked clubbing of the fingers and toes.

The diagnosis made on admission was: acute meningitis; congenital heart disease, probably pulmonary stenosis; old cerebral hemorrhage, with residual hydrocephalus and spastic paralysis of the left arm and leg; healed osteomyelitis of the left leg.

At the first lumbar puncture 10 cc. of cloudy fluid was obtained, and 10 cc. of antimeningococcic serum was injected intraspinally. Examination of the fluid revealed 6,700 cells per cubic millimeter and globulin (++++); the sugar content was apparently normal. Smears showed streptococci in short chains, and culture, green-producing streptococci.

The following morning only 5 cc. of fluid was obtained by lumbar puncture, and as the organism was not yet definitely identified, 10 cc. of antimeningococcus serum was again injected intraspinally. That afternoon only a few drops of serum was obtained by lumbar puncture. A cisternal puncture was performed and 30 cc. of cloudy fluid withdrawn. Since it appeared that an intraspinal block was present, 10 cc. of air under pressure was injected intraspinally through a lumbar needle. Thirty cubic centimeters of a 50 per cent solution of dextrose was given intravenously. The following morning, the fluid flowed freely after lumbar puncture, 25 cc. being obtained. Thirty cubic centimeters more of spinal fluid was drawn off by cisternal puncture, and a through and through cisternolumbar irrigation was performed with 100 cc. of physiologic solution of sodium chloride.

Daily lumbar punctures were then made with the patient on his side and the head and shoulders elevated on a pillow. The fluid was allowed to drain out until it dripped slowly, and from 15 to 20 cc. of air was then injected slowly through a syringe. After three minutes the syringe was removed; 20 cc. of additional fluid was usually thus obtained. Following this, an injection of an additional 15 cc. of air was given before the needle was removed. In this way from 50 to 60 cc. of fluid was removed at each treatment. At no time was there any unusual change in the pulse or the respiration. The patient was semicomatose and complained of no pain. This procedure was continued daily for nine days.

The temperature, which had varied from 102 to 104.5 F., suddenly dropped to normal on January 26 (ten days after admission) and remained about 100 F. except for one rise to 104 F. at the time when serum sickness developed. The mental condition gradually improved, and the patient appeared alert about two weeks after the onset of the illness. The spinal fluid cell count, which was 6,700 per cubic millimeter on admission, on January 26 (ten days after admission) was only 1,070. The fluid was sterile to culture seven days after admission and remained so. By February 22 (about five weeks after the onset of the illness) the child was free from all symptoms and signs of meningitis, but the spinal fluid cell

count still remained 75 per cubic millimeter. When the patient was discharged, about seven weeks after admission, the spinal fluid cell count was still 75 per cubic millimeter, but the patient had recovered entirely from the meningitis.

COMMENT

The most important factor in the treatment of meningitis is to provide adequate drainage. In the case just reported, the daily injections of air not only removed the intraspinal block and prevented new blocks from forming but, by displacing the fluid from the ventricles, aided materially in drainage.

Bingel [5] was the first to inject air into the spinal canal, employing it as an aid in encephalography. A number of European workers have since used this method in the treatment of meningitis. Nuske [6] treated five patients with meningococcic meningitis, three of whom recovered. Matovetskiy [7] treated fifteen patients with meningococcic meningitis, with eleven recoveries. Jauerneck,[8] after experimenting with various gases, concluded that acetylene is the best, since it is very soluble, being absorbed from the ventricles within three hours, and is slightly bactericidal and mildly sedative. I have been unable to find any reports by English or American authors of the use of air or other gases intraspinally in the treatment of meningitis.

SUMMARY

Two cases of streptococcic meningitis in which recovery followed are reported. In one of these there was spontaneous drainage of spinal fluid from the nose owing to a fracture of the skull. In the other daily insufflation of air intraspinally was employed to break up an intraspinal block and to aid drainage.

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5. Bingel, A.: Intraspinal Injection of Air (Encephalography), Deutsche med. Wchnschr. **47**:1492 (Dec. 8) 1921.

6. Nuske, M.: Die Behandlung der Meningitis cerebrospinalis epidemica durch Liquorausblasung, Monatschr. f. Kinderh. **58**:13, 1933.

7. Matovetskiy, I. I.: Treatment of Cerebrospinal Meningitis by Spinal Punctures and Fractional Insufflation of Air, Klin. med. (no. 7) **12**:1011 (May 26) 1934.

8. Jauerneck, A.: Erste Erfahrungen mit Meningitisbehandlung durch Azetyleneinblasung nach der Methode von Prof. Zeller, Deutsche med. Wchnschr. **59**:1790 (Dec. 1) 1933.

Progress in Pediatrics

PROGNOSIS OF CELIAC DISEASE

WITH A COMMENT ON THE HEMATOLOGIC CHARACTERISTICS

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During recent years several valuable contributions to the literature on celiac disease have been published. Bennett, Hunter and Vaughan [1] described in detail the records of fifteen cases in adults whose ages ranged from 16 to 57, which were undoubtedly instances of the disease described by Gee.[2] Their paper is, in fact, a consideration of celiac disease as observed when detected for the first time in adolescence or in adult life, although a perusal of the records shows that the disease had been present and untreated for many years. We have studied this paper with great interest, and we believe that it teaches the importance of recognition and thorough treatment of the disease at the time of life when it first develops, namely, during the early years of childhood, thus preventing the development of the degrees of disability present in these unfortunate persons. Although a form of steatorrhea known as non-tropical sprue may occur in adults and bear points of considerable similarity to celiac disease of childhood, from a clinical standpoint we believe that in any given case differentiation between the adult type of the disease (sprue) and the late and advanced stages of the juvenile form (celiac disease) is not difficult. Bennett, Hunter and Vaughan were able in the majority of their fifteen cases in adults to elicit from either the patient or the parents a history of rickets or "consumption of the bowels" in infancy; in one case only was there no history of the disorder in childhood. The insidious nature and progress in some cases of celiac disease, especially when it does not produce serious symptoms

From the Children's Hospital, Birmingham, England.

1. Bennett, T. I.; Hunter, D., and Vaughan, J. M.: Quart. J. Med. **1**:603 (Oct.) 1932.

2. Gee, S.: St. Barth. Hosp. Rep. **24**:17, 1888.

and signs in the earliest years of life, doubtless have accounted for the "chronic late" cases in which diagnosis had not been made in the early stages. The gradual stunting of development and the slowly progressive or intermittent nature of the symptoms and of various secondary effects, e. g., rickets, anemia, nutritional edema, tetany and diarrhea (or constipation), may not produce change, and when that is the case parents for a long time may fail to realize that a disease process is operating. They may, therefore, allow the celiac disorder to produce late effects; this appears to have been the course of events in the majority of the cases studied by Bennett, Hunter and Vaughan.

As Parsons [3] stated in a review of one hundred cases, the "onset of coeliac disease is usually insidious during the age period of nine months to two years," and, moreover, in our opinion it is far more common than is generally believed.

TABLE 1.—*Number of Patients with Celiac Disease Admitted to the Children's Hospital from 1922-1933*

Year	No. of Patients	Year	No. of Patients
1922	5	1928	28
1923	3	1929	17
1924	9	1930	15
1925	10	1931	16
1926	10	1932	17
1927	12	1933	29

In table 1 are recorded the number of patients with celiac disease admitted to the Children's Hospital from 1922 to 1933. The high value for the number of admissions in 1928 is explained by the fact that in that year many former patients were readmitted for reexamination and investigation of the fat content of the feces. Such factors do not affect the statistics for other years, which show the increasingly large number of cases recognized in the Midlands, probably owing to the increased dissemination of knowledge of the disease.

In the early years of life the clinical picture is sometimes striking when the child first comes under observation, and it seems clear that the disease must have been active for months at least, although advice may have been sought only for such acute symptoms as diarrhea, dehydration, wasting and tetany. A large number of children with celiac disease are, therefore, in poor physical state when first observed, and emergency measures, such as blood transfusion and the administration of fluids parenterally, including the intravenous use of solutions of dextrose, are frequently necessary. At this age period the disease has unfortunately a definite mortality rate.

3. Parsons, L. G.: Lancet **1**:61, 1931.

In table 2 is recorded the distribution on the basis of age of ninety-three patients with celiac disease admitted to the Children's Hospital in the five year period from 1928 to 1932. Fifty per cent were between 1 and 3 years of age. Moreover, all the fatalities occurred at the ages of 2 and 3 years. Many of these patients showed advanced atrophy at the time of admission, after months of fatty diarrhea and dehydration, with intercurrent infections of the respiratory tract and skin. The final factor in the outcome was usually bronchopneumonia, with signs of tetany in some instances.

The recognition of celiac disease in an infant about 1 year of age may be difficult, but attention should be directed to the physical outline, especially the atrophy of the gluteal and thigh muscles and the prominence of the abdomen, without ascites or enlargement of the viscera, and to the anemia and marked asthenia. At this age the stools may be easily recognized as bulky and fatty, but these characteristics are not uncommonly absent because of the small intake of food. A biochemical

TABLE 2.—*Data on Patients with Celiac Disease Admitted from 1928 to 1932*

	Age on Admission, Yr.													Total No. of Patients of All Ages
	½	1	2	3	4	5	6	7	8	9	10	11	12	13	
Total number admitted.....	1	6	20	23	5	12	9	6	3	3	2	1	1	1	93
Number showing satisfactory progress.....	1	6	12	20	5	12	9	6	3	3	2	1	1	1	82
Number who died.....	..	..	8	3	..	..	..	..	..	..	..	..	..	..	11

analysis of stools for five days is necessary for conclusive data. It is, however, of considerable importance to make a diagnosis as early in life as possible, since improper control may easily prolong the period of damage and endanger life. An intercurrent infection is often dangerous, the intolerance for fats is always aggravated, and diarrhea may be produced, especially in the younger children.

As it is observed in practice, celiac disease may present a variable picture. Constipation (with or without occasional bouts of mild diarrhea) may be the rule in some young patients, with one fatty stool every forty-eight hours. In some cases the chief clinical features are a moderate degree of infantilism, simple prominence of the abdomen and frequently hypochromic anemia. In an instance of this kind, however, especially when the condition is the result of a parenteral infection or occurs during extremely hot or cold weather, diarrhea with the passage of large, highly offensive fatty stools may develop and produce consequent rapid general physical deterioration. Anemia, although common in this disease and sometimes severe, is rarely the reason that a patient is first brought for examination.

On the other hand, celiac disease may not be recognized until well marked physical deformities have occurred, the result of osteoporosis, rickets and hypotonic musculature. The youngest patient we have observed at this stage was 5 years of age. More usually, the osseous changes are not apparent clinically until the age of about 7 years. It is evident in such cases that the celiac disturbance has been in operation for several years. We have observed children with advanced physical deformity who received prolonged orthopedic treatment before the essential intestinal disorder was recognized, and at least two patients first came under observation in the casualty department for fractures resulting from trivial trauma.

It is evident, therefore, that celiac disease is essentially a disease of childhood and that in a large percentage of cases it commences, as Parsons stated, in the first three years of life; it is apparent also that it is often overlooked or the child is regarded as suffering from abdominal tuberculosis. The condition may be regarded by the parents as rather unimportant, and the child may not be brought to the notice of the physician until considerable general changes have occurred; hence one cannot be surprised to find in this country a number of patients with the disease coming under observation for the first time in the later years of childhood, in adolescence or even in adult life, when considerable and even extremely advanced effects of the disorder, such as those reviewed by Bennett, Hunter and Vaughan, are present.

Our object in presenting this paper is to bring forward evidence to show that celiac disease responds remarkably well to proper therapeutic measures and that even in the cases in which on first observation acute complications or chronic secondary affects are revealed satisfactory improvement has usually been obtained. As previously stated, the case in which there is danger is usually one of a child about 2 years of age in which delayed recognition of the disease or acute intercurrent infection has deprived the patient of his last shreds of vitality.

In 1929 one of us (A. V. N.[4]) reported satisfactory results on subsequent observation in a number of cases of celiac disease studied in this country and at Boston (by permission of Dr. K. D. Blackfan); we have had ample opportunity to study other cases for a long period—in several instances for about thirteen years—and as many as possible are recorded in this paper.

The essential lines of treatment for celiac disease are fully recorded in the literature and in modern textbooks on pediatrics; it is not, therefore, our intention to make further comments on therapeutic measures, except so far as special points are mentioned in the description of the

4. Neale, A. V.: Birmingham M. Rev. **5**:77, 1930; Clin. J. **50**:313 (July 2) 1930.

recorded cases. Our essential objective is to show that with cooperation and continued supervision for long periods, even for years, good results can be obtained which amply repay the efforts expended. One case (case 2) will be outlined to show the tragic consequence of laxity in parental attention and treatment.

We propose to report the cases seriatim on the basis of the age of the patient when the last examination was made in 1933.

REPORTS OF CASES

CASE 1.—L. H., a woman aged 23, was the first child in a family of three children. All the others were well. She was never breast fed.

The patient was first seen in July 1925 at the age of 15 years. At the age of about 1 year she had "summer diarrhea." Since then she had had large, loose, "undigested" stools of a light color. There was no pain. The appetite was good. The patient did not seem to have grown since she was about 7 years old. The chest measured 24½ inches (62.2 cm.), the arms 16 inches (40.64 cm.) and the legs 25 inches (63.5 cm.). The height was 47 inches (119 cm.), and the weight 47 pounds and 10 ounces (21.66 Kg.). Rickets and osteoporosis were present. The patient was given a diet for the control of celiac disease.

In 1926 treatment with ultraviolet radiation twice a week and 1 tablet of irradiated ergosterol three times daily was commenced. This treatment had been maintained regularly.

The patient was examined in August 1928 at the age of 18¼ years. A regular diet free from fats had been maintained until twelve months previously when it was increased, but the patient still took few fats. Irradiated ergosterol was given regularly. The general condition was good. The abdomen was of normal size; the musculature was in good condition, and there were no rachitic signs or deformities. The mental development was normal. The teeth and eyes were normal. The secondary sexual development, which had been delayed until the last year or so, was progressing. Menstruation had not yet commenced. The mental outlook and general habits were also improved; a note of a private physician stated that the patient had been "quite childish before treatment commenced." The hair had ceased to grow until two years before but since then it had grown well. The skin was still "thin" and smooth. When the patient was given a diet low in fats, the stools were of more nearly but not quite normal color, and they were definitely increased on the intake of fatty foods. Roentgenograms of the bones showed atrophic structure of the type associated with celiac disease. Rickets was not evident. The teeth were normal roentgenographically.

In 1930 the patient had reached the age of 20, and the progress was good. She was at work regularly and appeared normal in every respect. She had continued an intelligent control of her diet, as it was thought that fatty foods still caused loose stools. She continued to receive ultraviolet radiation three times a week. She was at this time somewhat below the standard weight but was well developed. Menstruation commenced at the age of 18 and was normal. The hair was bright and shining, and the skin was "not so dry." Mental development had reached a normal standard.

Our last observation was made in 1933, when the patient was 23, and the only outstanding feature was that she was short (5 feet [152.4 cm.]) but of average weight (nearly 98 pounds [44.45 Kg.]). The teeth were poor but there was no other physical deformity. The bones were normal. She was able to take a full varied

diet; the stools macroscopically appeared normal, and the daily excretion of fat was well within physiologic limits. Sexual development proceeded normally, and the menstrual functions were regular. Since this woman is the only patient in our series who has passed the age of 21, we must conclude that the disease left its mark mainly in a shortened stature.

CASE 2.—R. D., a boy, was the third child in a family of six children, who lived in a healthy country district. All the other children were in perfect health. The patient was breast fed for nine months. At the age of 3 years diarrhea alba commenced.

In August 1925, when he was first admitted to the Children's Hospital, at the age of 10¼ years, his history showed that he had always been delicate. His attendance at school was irregular. He had large pasty foul stools. Treatment with

TABLE 3.—*Summary of Data in Case 1*

			Analysis of Stools*					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
7/15/25	15	Varied	52.6	22.2	30.4	10.1	12.0	....	...	47	48	Rickets; osteoporosis
7/ 7/25	15	Varied	58.1	30.3	27.9	14.2	16.1	....	...	47	48	Rickets; osteoporosis
7/24/25	15	Varied	52.0	26.2	25.0	16.3	9.8	....	...	47	48	Rickets; osteoporosis
8/23/25	18	Varied (trial)	25.9	7.4	18.6	7.4	0	....	...	55¼	78	Patient working; menstruation normal; rickets healed
1930	20	Free from fats	Good progress on celiac regimen									
1933	23	Varied	21.0	8.7	12.6	5.5	3.2	9	3	60	95	Normal appearance
			Daily excretion of fat only 1.1 Gm.									
Average normal values for the age.....										63	120	

* In this table and in tables 4–19 the values for fats are expressed in the total number of grams excreted in the stools in one day.

intestinal "antiseptics" and abdominal massage had proved of no benefit. At the age of 6 years he had been placed in splints. Two years later tetany had occurred periodically, and since that time he had been unable to walk. He had received no treatment for celiac disease.

On admission to the hospital he was unable to sit up. The skeleton showed marked deformity; both clavicles were bent; the humeri showed extreme bending; the femurs and tibias were curved, and scoliosis was present. These features and the abdominal distention are adequately shown in the accompanying photographs. The epiphyses were enlarged, and there were fractures of the radius and ulna and a marked rachitic rosary. The liver and spleen were not enlarged. Biochemical findings are recorded in the table and reveal the severe steatorrhea.

It was obvious that this boy was the victim of long-standing celiac disorder of a severe grade, with tetany and rachitic changes. He was only 38 inches (96.52 cm.) in height and weighed 30 pounds and 12 ounces (13.98 Kg.) at the age of 10.

From August to October 1925 the boy was given ultraviolet radiation without modification of diet. In this interval there was a slight but detectable increase in the calcification of the bones. The celiac state remained as before.

In October 1925 he was given a diet free from fats with a limited intake of carbohydrates, and the ultraviolet radiation was continued. During the next two months marked improvement continued, so that at the end of 1925 some fractures had healed. The rate of general bodily improvement was slow, however.

In January 1926, the same diet having been continued, irradiated ergosterol was administered. Progress continued to be good.

In August 1926 steady improvement was maintained.

In October 1926 the degree of healing of the bones was marked. A strict diet free from fats was maintained. The treatment with irradiated ergosterol and ultraviolet radiation was continued.

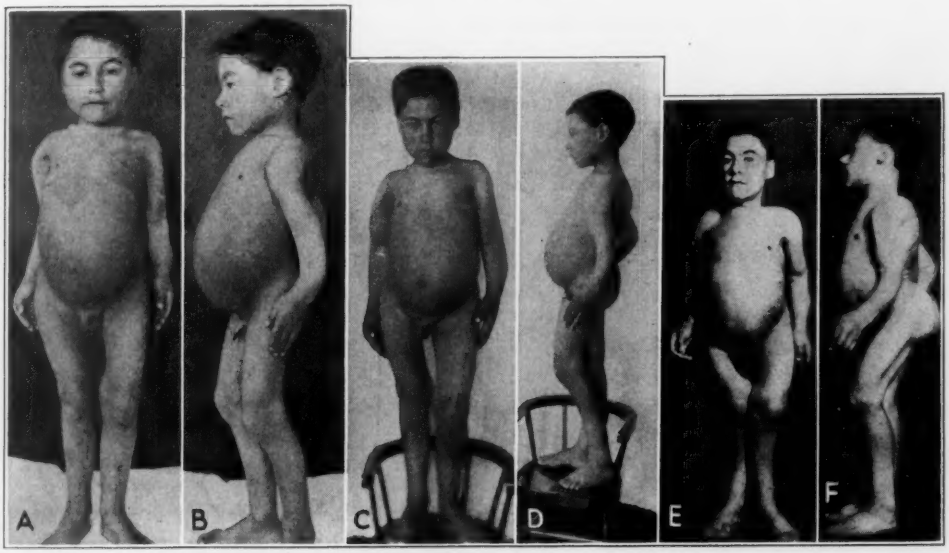

Fig. 1 (case 2).—Series of photographs of R. D. *A* and *B* were taken in 1925, *C* and *D*, in 1928, and *E* and *F* in 1933.

In March 1927 the bones showed roentgenographic features of healed rickets.

In October 1927 the patient was able to walk well and had grown 1½ inches (3.81 cm.) in eighteen months. There were great general improvement and conspicuous absence of bronchitis, which until this time had recurred frequently.

For five years before admission to the hospital and at the commencement of treatment the hair was harsh and grew very slowly (it required cutting only once in eighteen months). One of the first indications of recovery was that the hair became smoother, grew more quickly and had to be cut frequently. In November 1927 the hair was of normal texture and growth. Throughout the period of observation since 1925 the diet had been rigidly controlled.

In July 1929, at the age of 13½, the patient was attending school regularly. He was able to walk and eat well and was in good general condition. He was pleasant, happy and cheerful and of normal mentality. The general condition is illustrated in the photographs (fig. 1 *C* and *D*), which show the curvature of the

bones and the small stature. The thoracic viscera were normal. The abdomen was protuberant, and there was divarication of the rectus muscle. The general muscular tone was good. No abnormality of the abdominal viscera could be detected on palpation. When the patient was given a "third stage celiac diet" there was one stool daily of normal form and consistency. When he had a "cold," however, or a minor infection, there was a tendency to relapse of the diarrhea. Temporary experimental feeding of a full varied diet rendered the celiac state immediately manifest; the stools became bulky, fatty, offensive and more frequent. The urine was normal. There were no clinical indications of anemia. The teeth and eyes were normal. Roentgen examination showed complete healing

Fig. 2 (case 2).—Series of roentgenograms of the forearm of the patient whose photographs appear in figure 1. *A* was taken on Aug. 18, 1925; *B*, August 26; *C*, October 6; *D*, November 18; *E*, Jan. 12, 1926; *F*, March 10; *G*, March 24; *H*, June 8; *I*, September 1; *J*, October 28; *K*, March 23, 1927; *L*, July 13, 1928, and *M*, October 24, 1933.

of the rachitic changes in the epiphyses, but an osteoporotic structure of the matrix was observed, especially in the bones of the legs. The bones of the forearms revealed great improvement. A series of roentgenograms are shown. The height had reached 42 inches (106.68 cm.) and the weight 47 pounds (21.3 Kg.). The diet had been maintained, and treatment with 1 tablet of irradiated ergosterol twice daily and ultraviolet radiation was continued.

A comment in 1928 stated: "This is a case of severe celiac disease untreated for a long period, which has produced extreme changes in the bones and tetany. Rapid and progressive general improvement occurred during a dietetic regimen, and rickets was cured by the use of irradiated ergosterol and ultraviolet radiation. Although a growth of 4 inches (10.16 cm.) has occurred during the period of observation and treatment, the size and weight of the patient remain much below the average. There are biochemical evidences of persistence of the intestinal intolerance for fats but improvement is shown. Restoration of the calcium content of the serum to normal or to higher than normal values, such as are not uncommon during intensive vitamin D therapy, is indicated. Careful supervision of the patient is proceeding."

In January 1931 the patient failed to appear for observation. A letter from his mother stated: "He has not grown much but is in good health."

Further news of the patient was not obtained until 1933, when he was finally induced to attend the hospital. The examination at this date revealed the tragic effects of cessation of medical control. The photographs (fig. 1 *E* and *F*) and the roentgenogram (fig. 2 *M*) reveal the relapse of the condition and the general deterioration, which was only too evident. He had grown only 3 inches (7.62 cm.) and had gained only 19 pounds (8.6 Kg.) in five years. The calcium content of the blood had decreased to 7.5 mg. per hundred cubic centimeters, and the phosphorus content to 2.6 mg. The diet during this period had been unrestricted, and the stools were again loose, fatty and offensive. He had received no special therapy since 1928, with the exception of Marmite. Marked rickets was again present; osteoporosis had progressed, and as a consequence the skeletal deformity had been increased to an even more marked degree than when the first observation was made. The sclerotics were blue and the teeth carious.

To sum up, diagnosis was delayed until the child was 10½ years of age, but with the commencement of treatment improvement occurred. Sexual development and the appearance of puberty had been normal, but the rest of the development had been poor. This emphasizes the need for early diagnosis and treatment of celiac disease. This case ultimately proved the most disappointing in the whole series. It was, in fact, the only instance of failure. While in 1928 the patient showed evidence of general improvement, with every likelihood of continued satisfactory progress, all the good results so anxiously striven for and obtained at that time were lost, and the boy reverted to his former bad condition, with marked changes in the bones and active rickets. All this may be explained as the result of lack of continued care at home and proper medication. It emphasizes the adverse results of lack of attention in a case of an otherwise easily controlled and remedial disease.

CASE 3.—D. B., a girl, was the only child. The patient did not come under control at the Birmingham Children's Hospital until the age of 7¾ years, although it was evident at that time that she had long suffered from the condition. She had "always been short for her age" and had had a large abdomen for a long period. Deformities had occurred, and femoral osteotomy had been performed. Her condition was immediately recognized as celiac disease. The stools were large and typical of the condition. Roentgenograms of the long bones showed rachitic changes in the epiphyses and osteoporotic structure. Biochemical investigation confirmed the clinical findings. She was only 41 inches (109.22 cm.) in height (the average height for a child of the age of 5).

The observations just mentioned were made in February 1923. The child was not observed again until May 1928. The parents had apparently failed to adhere to instructions and had not brought the child to the hospital in the intervening

years. The mother stated, however, that owing to diarrhea the child had voluntarily restricted the intake of fat. Progress, of course, had been poor, and the mother had taken the child to an orthopedic clinic where no treatment for celiac disease was given but surgical irons were applied in an attempt to correct the deformities of the lower limbs.

TABLE 4.—*Summary of Data in Case 2*

Date	Age, Yr.	Diet	Analysis of Stools: Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Analysis of Blood: Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
9/ 7/25	10½	Varied	60	21.0	35.0	12.6	8.0	6.0	3.0	38	30¾	Tetany; rickets; general poor condition
10/21/25	10½	Celiac (stage 2)	21	13.0	18.0	6.2	7.0	....	...	38	30¾	Treatment with irradiated ergosterol and ultraviolet rays commenced
6/29/26	11½	Celiac (stage 2)	25	9.2	16.3	4.0	5.2	....	...	..	..	No tetany; improvement
10/29/26	12	Celiac (stage 2)	18	3.0	15.0	....	....	9.3	3.4	..	..	Marked improvement in general condition and in bones
3/23/27	12½	Celiac (stage 2)	28	18.0	10.0	12.3	5.8	10.5	4.4	39½	..	Progressive improvement
7/13/28	13½	Varied (trial)	38	18.6	19.5	11.9	6.7	12.3	...	..	..	High calcium content of the blood; healed rickets
7/28/28	13½	Celiac (stage 3)	20	7.0	13.0	5.4	2.3	....	...	42	47	Good general health; patient attending school (fig. 1 C and D)
Jan. 1931		Failure to appear for observation. The mother wrote: "He has not grown much but is in good health."										No knowledge of what care the boy received
10/24/33	18	No control; "anything," according to the mother	One large, loose stool daily					7.5	2.6	45	66	Photographs (fig. 1 E and F) and roentgenogram (fig. 2 M) show relapse and increased deformity; marked retrogression and recurrence of rickets due to failure of supervision

When the patient was observed in May 1928, at the age of 13, the general condition was extremely bad; she was unable to walk unsupported; she was markedly dwarfed, being only 45 inches (119.38 cm.) in height and weighing 50 pounds (22.7 Kg.). As shown in the photographs (fig. 4 *A* and *B*), there were deformity and marked swellings of the epiphyses, with curvatures of the long bones. The teeth were poor and obviously deficient in structure. The musculature was poor. The nervous system was normal, and no tetany was present. The urine was normal. There were daily stools of the type associated with celiac

disease. Bacteriologic examination of the feces gave normal results. The mental development was normal. Roentgenograms showed a marked increase in the rachitic changes as compared with the findings on examination in 1923. It was

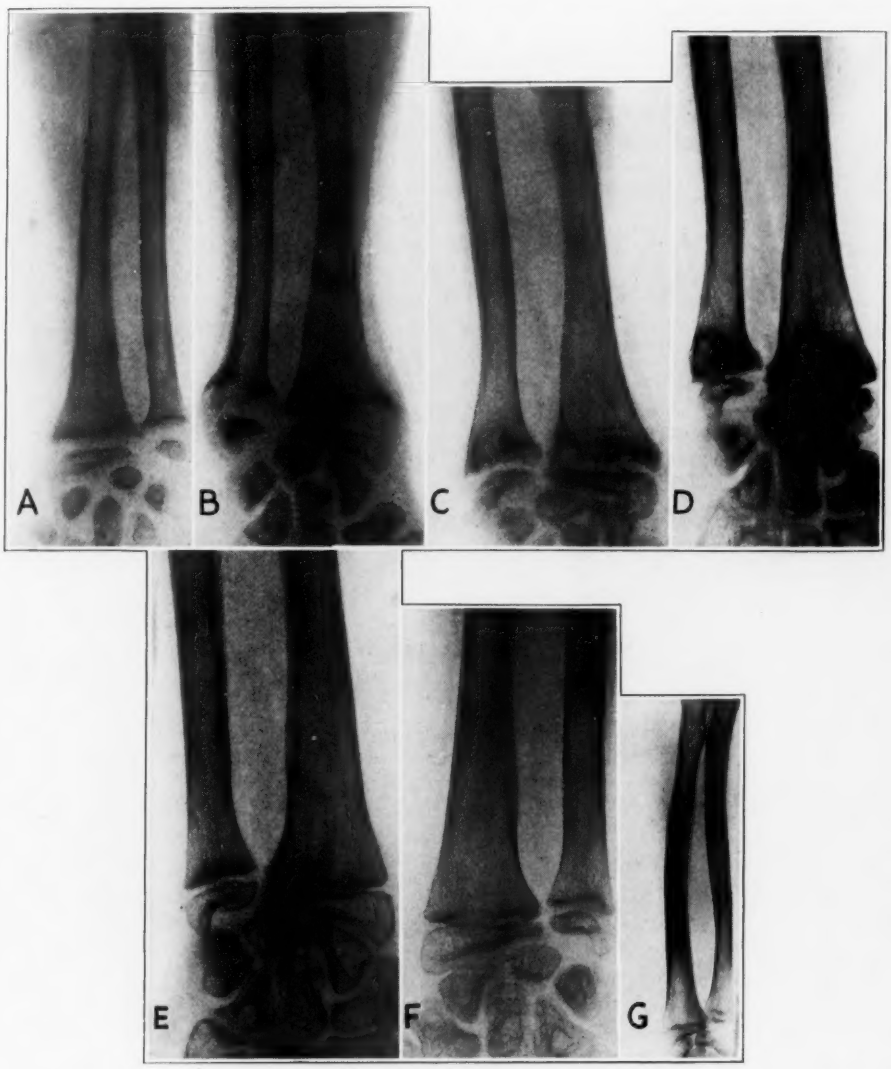

Fig. 3 (case 3).—Series of roentgenograms of the forearm of D. B. *A* was taken on Feb. 5, 1923; *B*, May 11, 1928; *C*, Aug. 3, 1928; *D*, Sept. 17, 1928; *E*, April 18, 1929; *F*, Nov. 17, 1930, and *G* in 1933.

obvious, therefore, that this girl had been the victim of improper attention and had passed through several years of unnecessary suffering. It is likely that this condition would have persisted had not members of the staff of the Children's

Hospital inquired after the child. Biochemical studies revealed intolerance for fats such as was present in 1923, which had apparently in no way improved. Metabolic determinations showed well marked steatorrhea.

In May 1928 dietetic control was instituted, and irradiated ergosterol was given daily, with ultraviolet radiation three times a week. Careful control of the patient was maintained from that time, and in August 1928 the general condition showed remarkable improvement; a gain of 2 pounds (90.7 Gm.) had occurred, and roentgenograms revealed rapid healing of the rickets. She was then able to walk unaided. The muscular tone, general physique and demeanor showed decided improvement.

A comment in 1928 stated: "This case illustrates the disastrous effects of the neglect of treatment of celiac disease and the rapid response to systematic treatment."

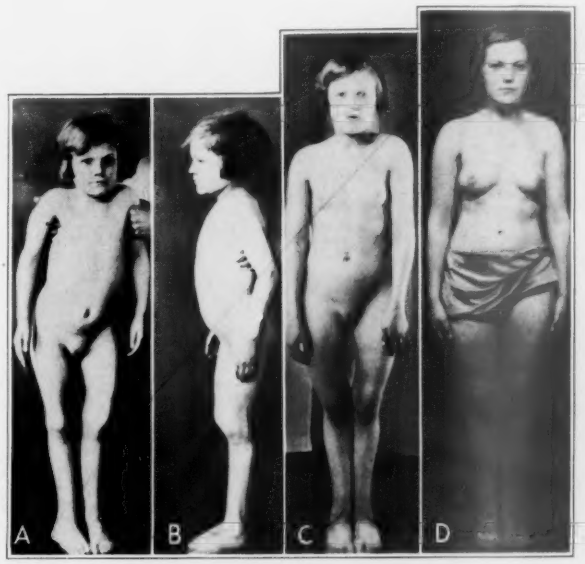

Fig. 4 (case 3).—Series of photographs of D. B. *A* and *B* were taken in 1928; *C*, in 1930, and *D*, in 1933 at the age of 18.

In 1930 it was evident that proper home supervision of the patient had been continued since 1928. The diet had remained strictly free from fats, and regular daily administration of irradiated ergosterol and ultraviolet irradiation three times a week had been continued. The stools were of normal appearance, and there was no diarrhea. The general physical outline had improved (fig. 4 *C*) and the deformities were disappearing. The splints had been discarded in 1929, and the patient was able to walk by herself in comfort. She had gained 23 pounds (10.4 Kg.) and had grown 8 inches (20.32 cm.) in the past two years. Roentgenograms of the bones showed improved structure and complete healing of the rickets. The teeth were normal. The hair was much improved in quantity and quality.

Our final record in 1933 revealed a very satisfactory result. The photograph (fig. 4 *D*) illustraes the physique of the patient at the age of 18. The deformities

had disappeared. She was bright and alert and worked regularly. Menstruation commenced at the age of 16 and was physiologic. She received an ordinary full diet, and there was one macroscopically normal stool daily. No diarrhea was present. She had continued her education and was of normal intelligence.

CASE 4.—M. R., a girl, was the second child of a family of two children. In 1919, at the age of about 4 years, she began to have troublesome diarrhea with large, unformed, fetid, pale stools. This symptom varied in degree, with periods of relative improvement and severe exacerbations. No vomiting occurred. The child did not gain in weight. At the time of observation in June 1920 there were daily as many as three stools typical of those associated with celiac disease. The weight was only 23 pounds (10.4 Kg.) and the height 35 inches (88.9 cm.), each value being considerably below the average for a child of the age of the patient. The next record stated that the patient was readmitted to the hospital in March 1921 with tetany. Rickets was present. The abdomen was distended but tympanitic; diarrhea continued and extremely fatty stools were passed (there had been

TABLE 5.—*Summary of Data in Case 3*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
1922	7¾	Varied	32	15.4	....	....	....	....	...	41	..	Rickets
5/ 1/28	13	Varied	35	16.7	18.3	15.4	1.2	....	...	..	..	
5/ 5/28	13	Varied (trial)	41	35.6	3.6	25.0	6.0	9.5	3.2	45	50	Marked rickets
1930	15½	Restricted fats	Appearance normal; no diarrhea					....	...	53½	77	Rickets healed
1933	18½	Varied	One normal stool daily					10.5	3.4	57	114	See figs. 4 D and 3 G
Average normal values										62	105	

no dietetic control). After a short sojourn in the hospital on a regimen for relief of celiac disease improvement occurred, and the diarrhea was relieved. A report in June 1924 stated that the child still had as many as three stools daily but that the nutritional state was somewhat improved. She was not growing perceptibly. No further hospital supervision took place. The dietetic control was irregular, and reexamination of the child in February 1925 revealed the results of improper attention. She remained markedly undersized, although she was very intelligent. She was unable to walk. The stools were pale and fatty. Rachitic signs were present, and genu valgum was well marked. The epiphyses were swollen. Roentgenograms showed rarefaction of the trabecular structure of the bones and rachitic changes in the epiphyses. Osteotomy for the relief of genu valgum was considered, but a surgeon noted that the bones were too atrophic to warrant the procedure. From this time proper dietary control was obtained under direct hospital supervision. A diet free from fats was instituted, and regular treatment with ultraviolet radiation was given. Eight weeks later it was obvious that marked improvement was taking place. The rickets showed roentgenographic evidence of healing. At the end of 1925 the rickets had completely healed, and the child was able to walk again comfortably. Observation throughout 1926

revealed steady progress, and growth was evident. The patient was able to attend school again. The genu valgum had diminished. Treatment with a fat-free diet and radiation had been maintained satisfactorily.

In August 1928, at the age of 13, the height was 5 feet and 1¼ inches (156.2 cm.) and the weight 75 pounds (34 Kg.). The condition is shown in the photograph (fig. 5 *A* and *B*). Physical improvement was marked, and there was no deformity except slight genu valgum. Rickets was completely healed, and roentgenograms showed almost normal density of the bones. The teeth were good. The abdomen showed no abnormalities. The gluteal outline was normal. No abnormality of the viscera was detectable. There was one stool daily, which was formed and of good color. The urine was normal. The patient was then happy, active and intelligent. There was a considerable amount of subcutaneous

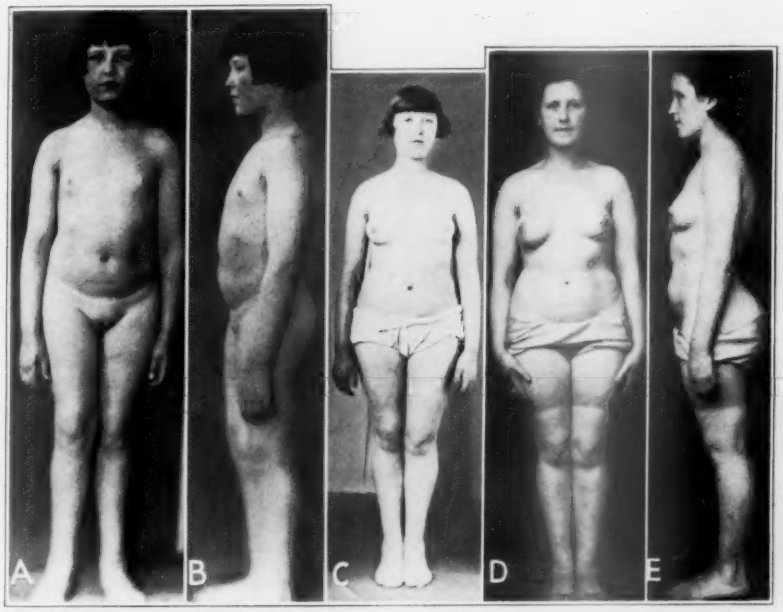

Fig. 5 (case 4).—Series of photographs of M. R. *A* and *B* were taken in 1928 at the age of 13; *C* in 1930, and *D* and *E* in 1933, at the age of 18.

fat over the body, giving a physical outline resembling that in Fröhlich's syndrome. Biochemical examination showed that the excretion of fat was almost within normal limits when the patient was given an ordinary varied diet.

A comment in 1928 stated: "This patient with celiac disease has been under observation for about eight years. Until 1925 the condition was improperly controlled, with the result that marked general deterioration developed. Since the institution of rigid control of the diet and ultraviolet radiation, good progress has been maintained; the rickets and deformities were corrected; the growth was stimulated, and the patient is now practically normal both physically and mentally."

Reexamination of the patient in 1930 revealed first class progress (fig. 5 *C*). She had attended school regularly and was in the senior class. The gains in height and weight were good. She was 15½, and normal menstruation had

commenced at the age of 14. When she was given an ordinary mixed diet there was no diarrhea; normal tolerance for fat was, therefore, established. The bones were normal.

In 1933, at the age of 18, there was no doubt of her physical well-being (fig. 5 *D* and *E*). She was a heavy-set girl. Her general health was good. She was working regularly. There was abundant subcutaneous fat, which was evenly distributed. The bones and teeth were normal. Ordinary food had no ill effect. The stools, one daily, were of normal appearance. The patient had grown rapidly during the past three years and weighed 126 pounds (57.15 Kg.).

TABLE 6.—*Summary of Data in Case 4*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
June 1920	5	Varied	Celiac type of diarrhea					....	...	35½	25	Severe grade of celiac disease
March 1921	6	Varied	Four stools of the celiac type daily					....	...	..	..	Tetany; rickets
2/ 4/25	10	Free from fats	18.7	2.4	16.3	2.4	0	....	...	40	37½	Rickets; severe fatty diarrhea
4/ 7/24	10	Free from fats	15.7	1.8	13.9	1.8	0	8.4	4.4	..	..	Ultraviolet radiation; celiac diet
10/23/25	10½	No diarrhea when the patient was on a fat-free diet								41½	41	Rickets healing; good progress
March 1927	12	Free from fats	....	....	....	....	....	10.0	5.0	..	..	Rickets healed; good growth
April 1928	13	Restriction in fats	19.4	4.2	15.2	2.6	1.6	12.3	4.3	51¼	75	Adiposity (fig. 5 A and B)
Oct. 1930	15½	Varied	Normal stools; normal tolerance for fats					....	...	58½	113	No deformity (fig. 5 C)
July 1933	18	Varied	Normal appearance					9.0	4.0	60	126	Excellent physique (fig. 5 D and E)
Average normal values										62	106	

CASE 5.—M. G., a girl, was the first child of a family of two children. She had been breast fed for fourteen months. Symptoms and signs of celiac disease developed soon after she was weaned and given a varied diet, at the age of 14 months. The child was first observed at the Children's Hospital in November 1920, at the age of 4 years. The diarrhea had persisted since its onset. The general health was poor. She was languid and obviously underweight and ill nourished. Two large, offensive, highly fatty stools were passed daily. There was no detectable abnormality of the viscera.

In February 1921 a diet for the relief of celiac disease was commenced; the amount of proteins and carbohydrates was gradually increased, but the fats were eliminated. Several months later improvement in every way was marked. The diet was gradually increased, with careful observation of the tolerance of the patient, until eventually in 1927 the child was able to take a moderately varied

diet, including a little butter and whole milk, without recurrence of symptoms. Good progress had been the marked feature in this case, although entrance to school was delayed until the age of 7 on account of the physical condition.

In May 1928, at the age of 11, the general nutrition and musculature were good. The abdomen was flat. There was no deformity. A roentgenogram showed somewhat osteoporotic structure of the bones but no rickets. Biochemical examination when the child was given a full, varied diet revealed no increase in the fat content of the stools, and the readings for the calcium and inorganic phosphorus contents of the blood were normal. The height was 55 inches (34.62 cm.) and the weight 53 pounds (24 Kg.).

A comment made in 1928 stated: "This is an apparently mild form of celiac disease treated early and continuously by dietary control only, which has given good results."

TABLE 7.—*Summary of Data in Case 6*

			Analysis of Stool					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
11/29/24	6½	Varied	36	10.0	26	....	....	....	...	38	31	Typical celiac disease
7/18/28	10½	Restriction of fats	23	9.5	13	5	4.5	10.1	4.5	45½	49	Careful supervision for 3 years
1930	12	Restriction of fats	Diarrhea if amount of fat is not strictly controlled					....	...	33½	77	Physique and growth good
1933	15	Full and varied	Normal; only 1.5 Gm. of fat excreted daily					9.0	3.0	63	109	Appearance normal; mentally and physically active
Average normal values										61	106	

In 1930 the child was again carefully examined and found to be progressing well. The weight was 84 pounds. (38.1 Kg.) and the height 61 inches (154.94 cm.). The stools appeared normal.

In 1933, at the age of 16, the height was 63½ inches (161.29 cm.) and the weight 104 pounds (47.15 Kg.). The physique was good. The teeth and bones were normal. The stools were normal. The calcium content of the blood was 10.6 mg. and the phosphorus content, 2.9 mg. per hundred cubic centimeters. Development seemed to have been good; the outward appearance was normal, and there was no evidence of celiac disorder. The onset of menstruation occurred at the age of 14.

CASE 6.—H. B., a girl, was the thirteenth child of a family of fourteen children. All the others were well. She had been breast fed one month and was then given cow's milk.

In November 1924, at the age of 6½ years, she was first observed at the hospital. For two years the child had had diarrhea, with several putty-like stools a day. The abdomen was large, but there was no enlargement of the viscera. The chest was normal. The stools were typical of those associated with celiac

disease. The height was only 38 inches (96.52 cm.) and the weight 31 pounds (14.1 Kg.). The abdomen measured 20¼ inches (5.44 cm.). The child was given a diet consisting of lean meat, skimmed milk, etc., which was continued regularly for three years (until 1927). During 1928 she had taken small amounts of fresh butter.

In August 1928, at the age of 10, there was no diarrhea, and the stools were much improved, but any overfeeding of fat still caused temporary "relaxed bowels." The child had been growing well during the last twelve months. The general health was much improved. She had attended school regularly, and the mental development was normal. No rickets or deformities were present. The teeth were in good condition, and all were present. The eyes, musculature, chest and

Fig. 6 (case 7).—Series of roentgenograms of the forearm of S. P. *A* was taken in June 24, 1927; *B*, Nov. 9, 1927; *C*, Aug. 12, 1928, and *D*, Jan. 14, 1930.

outline of the abdomen were normal. Examination of the urine gave negative results. There was no fever. The feces were of normal color and consistency (when the patient was given a low fat diet). Roentgenograms showed that the bones were normal. The height was 3 feet and 9½ inches (115.57 cm.) and the weight 49 pounds (22.25 Kg.). The abdomen measured 22 inches (55.88 cm.). The child had received no ultraviolet radiation or drugs. She lived in a country house and was "considerably exposed to sunshine each day."

Observation in 1930 revealed good progress and adequate control of the disease. The patient had remained regularly on a diet restricted in fats. Diarrhea still occurred if more than small amounts of fat were allowed. The physique was

good, and the gluteal and general musculature was much improved. The teeth were good. The growth was steadily maintained. No auxiliary supply of vitamins had been given. The bones were normal.

In 1933 the patient had reached the age of 15. She was active and bright. The posture was good. She was growing well. Roentgen examination of the bones showed a normal condition. At the time of writing she was receiving an ordinary diet, but the intake of fat was still low. The stools were normal. The excretion of fat in the stools was only 1.5 Gm. per day (the average normal amount for a healthy person). Menstruation commenced at the age of 14 and was regular and physiologic.

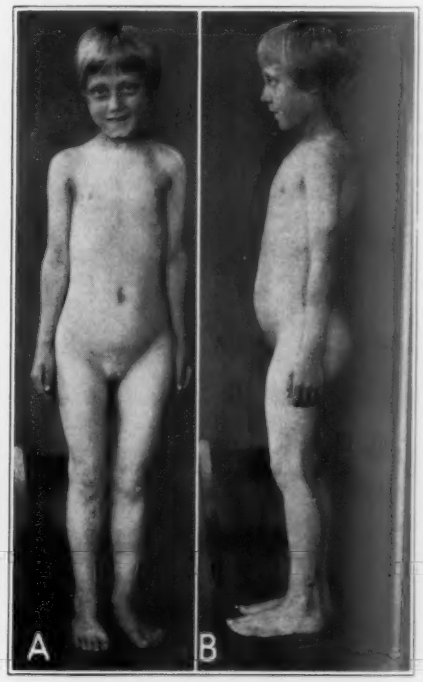

Fig. 7 (case 7).—Photographs of S. P. taken in July 1928, at the age of 12, after two years of treatment.

Case 7.—S. P., a girl, was an only child. The parents were healthy. She had never been breast fed but had been given Allenbury's Food[4a] in infancy.

The child first came under observation in June 1927, at the age of 10½ years. She was brought to the hospital at that time for fracture of the right radius, which had occurred apparently without much violence. Until this time medical supervision of the child had not been sought, although the mother stated that the child had worn irons for a deformity of the legs at the age of 8. The mother had

4a. Allenbury's Food is a proprietary food for infants, used chiefly in England. It consists of malted cereals combined with dried milk powder. It is diluted with water to the desired strength.

noticed that the child was not developing as she should and that since babyhood she had passed loose, pale, offensive stools.

General examination of the patient revealed a poorly developed, pale girl, much undersized for her age. She presented a rachitic appearance, with slight genu valgum and a marked rachitic rosary. Rachitic changes in the skull were present. The epiphyses were greatly enlarged. The teeth were in a poor condition, and several were carious. The abdomen was protuberant, but no other abnormal signs were noted. Examination of the thoracic viscera showed a normal condition. There was no tetany. The stools were typical of celiac disease, and biochemical examination showed a high content of fat. No abnormal bacteria were found in the stools. Stercobilin was present. The child weighed only 40 pounds (18.1 Kg.). It was recognized as fortunate that she had been forced to attend the hospital with the fractured forearm; otherwise, she would not have received attention for the underlying celiac disease.

TABLE 8.—*Summary of Data in Case 7*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
June 1927	10½	Varied	53.5	71.8	29.0	....	....	9.8	3.3	..	40	Active celiac disease; rickets; fracture; deformities
July 1927	10½	Free from fats	28.0	....	....	....	....	....	...	..	..	Ultraviolet radiation; ergosterol; control of diet
Aug. 1928	11¾	Moderate amount of fat	44.3	16.8	27.5	12.8	4	10.8	4.8	46½	46	Great general improvement; rickets healed
Sept. 1930	14	Restriction of fats	Usual appearance normal; seasonal diarrhea					....	...	52½	68	Good physical outline

In July 1927 treatment was commenced with a diet high in protein and moderate carbohydrate content and relatively free from fat. It was well received. Treatment with ultraviolet radiation and 1 tablet of irradiated ergosterol three times daily was commenced also at this time. This regimen was maintained.

In August 1928 the general progress was good. The weight had increased to 46 pounds (20.9 Kg.). The musculature and gluteal outline showed marked general improvement. The teeth were decidedly improved, and roentgenograms showed complete healing of the rickets and diminished osteoporosis of the bones. The abdomen had become less protuberant. No abnormalities of the viscera were present. When the child was given the "celiac" diet the stools remained satisfactory, but when she received an ordinary varied diet they rapidly became highly fatty. Biochemical data showing these phenomena are given in the table.

A comment in 1928 stated: "This is a case of prolonged neglect of celiac disease with rickets and fractures. Rapid cure of the lesions of the bones and great general improvement took place with dietetic treatment and auxiliary vitamin medication. The celiac state is still in evidence."

In 1930, at the age of 14, the patient was 52½ inches (133.35 cm.) in height and 68 pounds (30.8 Kg.) in weight. In physique she was sturdy. There were no deformities. The teeth were good. The diet had gradually been increased, but the restriction of fats was continued. Cold weather seemed to cause diarrhea, the stools being otherwise of normal appearance. Treatment with ultraviolet radiation was continued.

CASE 8.—L. M., a girl aged 3 years, was the fourth child of a family of six children. In August 1923, at the age of 3 years, diarrhea commenced, with from two to three large, light-colored, fetid stools a day. There was no melena. The abdomen was swollen. There was no pain. The child was delicate and pale; she was undersized and tired easily. She was given a light diet with a low content of fat.

The patient was observed again in August 1928, when it was learned that in 1927 she had been in an open-air home for convalescent patients for nearly a year

TABLE 9.—*Summary of Data in Case 8*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
July 1923	3	Varied	53.0	....	....	....	....	....	...	..	..	Typical celiac disease
Oct. 1927	7½	Varied (test)	49.0	....	....	....	....	....	...	..	..	Careful treatment maintained
Nov. 1927	7½	Varied	60.0	....	....	....	....	....	...	..	..	
Aug. 1928	8½	Varied	14.4	7.5	6.9	3	4.5	12	5.1	45	42	Rapid improvement
Nov. 1930	10½	Varied	Normal					....	...	..	..	
July 1933	13	Varied	Normal					9	4.7	53	63	Good physique

and had improved greatly. No ultraviolet radiation or drugs were prescribed, but open-air life and much sunshine. She was growing better and had gained probably 3 inches (1.62 cm.) during eighteen months. She had also gained in weight.

In 1930, at the age of 10¼, a clinical examination showed that the progress was good. The dietetic control had been somewhat modified, and the intolerance for fats had apparently ceased. The stools were normal.

In 1933, at the age of 13, the clinical examination gave normal results. The child was bright, and the posture was good. The functions of the alimentary canal were normal.

CASE 9.—J. B., a girl, was the eighth child of a family of twelve children. All the others were well and normally developed.

The mother of the child stated that the patient had walked normally at the age of 1 year but that since that time growth and general development had been poor as compared with that of the other children, who were conspicuously healthy and well formed. During the six months prior to admission to the hospital the

child had walked badly and with difficulty. For an indefinite period the stools had been pale, fetid and frequent.

When observed in May 1927, at the age of 7, the patient appeared to be only about 4. The abdomen was prominent but soft. Rachitic features, such as bossing of the skull and genu valgum of the lower limbs, were pronounced. No abnormality of the viscera was found. The urine was normal. The stools were typical of those seen in celiac disease. Roentgenograms of the long bones showed marked rickets and osteoporotic structure. The weight was only 28 pounds (12.7 Kg.). Biochemical studies of the feces revealed marked characteristics of

Fig. 8 (case 9).—Series of roentgenograms of the forearm of J. B. *A* was taken on July 8, 1927; *B*, Feb. 16, 1928, and *C*, Sept. 7, 1933.

celiac disease, and the calcium and phosphorus contents of the blood serum were markedly abnormal. No tetany was detected. In June 1927 dietetic treatment and administration of irradiated ergosterol were commenced. Owing to the fact that the mother of this child had exophthalmic goiter, considerable difficulty was found in insuring proper care of the child at home. The diet had been adhered to fairly well, however, and irradiated ergosterol was given periodically.

In 1928 investigation showed that the child was growing and walking better and that she was attending school regularly again. The general state was only moderately good, however, and she was not doing as well as she should. The

abdomen was still prominent. On the prescribed diet the stools were satisfactory. Owing to the general laxity of maternal attention, the child had taken a full varied diet for several weeks with a prompt relapse of the diarrhea and general state. The child was readmitted to the hospital for observation of this process. Roentgenograms showed progressive improvement in the rickets, but complete cure had not yet been obtained. There had been a gain of 6 pounds (2.7 Kg.) and a few inches in height during the twelve months.

A comment made in 1928 stated: "This is another case illustrating the slow but steady course of celiac disease when it is undetected and untreated. It is strange that the mother should not have sought advice about the child earlier. As in the other cases, improvement occurred when advice was followed, but the condition of the mother had not allowed the child to receive as good control as is usual, and consequently progress had been slower."

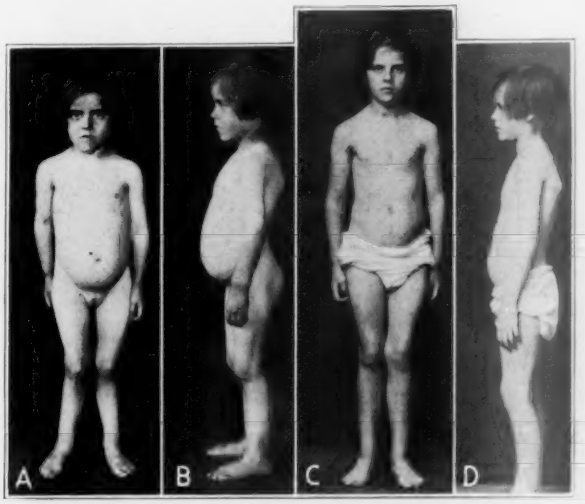

Fig. 9 (case 9).—Series of photographs of J. B. *A* and *B* were taken in 1928, and *C* and *D* in 1933, at the age of 13.

In 1933, at the age of 13, the girl had made good progress. Her physique was satisfactory (fig. 9 *C* and *D*). The genu valgum was much less marked, and the posture was good. The shape of the head was good, and the teeth were normal. Growth had been good in the past few years. All the roentgenographic signs of rickets had cleared, and the structure of the bones was normal. A full diet had been allowed for the past year, and a normal active life was carried on. The patient had attended school regularly for several years. Puberty had not yet been reached.

Case 10.—A. E. R., a boy aged 5 years, was the fourth child of a family of five children. All the others were healthy. He was never breast fed, as all the other children had been.

For three years prior to February 1926 the boy had been ill with diarrhea and had not gained weight satisfactorily. He appeared fairly well but was obviously undersized. The abdomen was full and soft. The stools were large, pale and

semiformed and of the type seen in celiac disease. The weight was 29 pounds (13.2 Kg.).

In April 1926 the patient was still losing weight, having lost 1½ pounds (680 Gm.) in two months. There were three stools a day, which were of the type seen in celiac disease.

In September 1926 he was given a diet for the relief of celiac disease; irradiated ergosterol was administered each day and ultraviolet radiation regularly twice a week (the irradiation was continued for one year).

A comment in August 1928 stated: "The patient has not grown much during the last twelve months, but his general condition is improved. He appears much stronger. He takes food well. There is movement of the bowels regularly once daily; the stools are formed and not fetid. The abdomen is still somewhat enlarged but is otherwise normal. The teeth and eyes are normal. No rachitic signs or deformities are present. The chest is normal. Examination of the urine

TABLE 10.—*Summary of Data in Case 9*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
5/25/27	7	Varied	46	25	21.0	21.0	3.5	7.8	1.5	..	28	Rickets; genu valgum
8/25/27	7¼	Free from fats	..	..	....	....	....	10.8	2.8	..	..	Treatment after 3 months
9/20/28	8¼	Free from fats	23	9	14.5	4.5	4.5	11.2	4.8	38	34	Progress good
1931	11	Restricted	Appearance normal					....	...	44½	48	Progress good
1933	13	Full	Appearance normal					9.6	6.6	49	54	Progress good
Average normal values										57	84	

gave normal results. Roentgen examination shows bones of the type associated with celiac disease. No rickets but osteoporosis with transverse striae is evident."

In 1930, at the age of 9, the stature was short, but the general progress was satisfactory. Dietetic control had been continued, and fats were strictly omitted. The patient had taken irradiated ergosterol regularly. The stools were satisfactory; the size of the abdomen was reduced, and the muscles were strengthened. Atrophy of the gluteal muscles had disappeared. The edge of the teeth revealed a slight defect. The clinical and roentgenographic appearance of the bones was normal. The boy had grown 4 inches (10.6 cm.) in two years, and he was bright and active. The hair was still thin.

In 1933, at the age of 12, investigation showed that the diet had been somewhat improperly controlled during the past two years, a quantity of fatty foods having been allowed with the result that occasional stools of the type seen in celiac disease and diarrhea were produced. The administration of irradiated ergosterol was continued. The growth had been slow—only 1 inch (2.54 cm.) in several months. The physical outline, however, had further improved, but the abdomen was still prominent; the gluteal muscles were not normally full, and general hypotonia of the muscles was present. The teeth were not good. Roent-

genograms of the bones were normal. From all appearances celiac disease was still moderately active in this case. The usual postural characteristics and delayed development were present as long as careful dietetic and general control was neglected. The progress would have been better if the fat-free diet had been adhered to constantly.

CASE 11.—G. P., a boy, had an attack of diarrhea in July 1923, at the age of 2 years. The stools were large, pale and offensive. There was occasional vomiting.

The patient came under medical observation in March 1926. He was wasted, undersized and underdeveloped, with distention of the abdomen but no ascites. The clinical diagnosis was an early stage of rickets. The weight was only 20 pounds (9.1 Kg.) at the age of 5. A dietetic regimen with no fats was commenced and carefully maintained. Ultraviolet radiation was given three times a week.

TABLE 11.—*Summary of Data in Case 10*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
Feb. 1926	5	Varied	44	17	26.5	11.0	6.2	....	...	..	29	Marked infantilism
March 1926	5	Varied	47	22	25.0	11.2	4.2	....	...	37	..	
Aug. 1928	7½	Free from fats	17	14	12.6	1.5	3.0	10.6	5.6	38½	33	Slow progress
1930	9	Free from fats	Stools satisfactory					....	...	42½	44	Good progress
Aug. 1933	12	Mixed	Occasional diarrhea					9.0	3.5	45	47	Infantilism still evident

In 1928, at the age of 6½, the progress was good. The general condition was much improved. The swelling of the abdomen was less marked, and the musculature was more fully developed. The viscera were normal. The stools were darker and smaller and were inoffensive. The weight had increased to 31 pounds (14.1 Kg.) and the height to 38 inches (96.52 cm.).

The medical supervision of the boy was maintained, and in 1930 at the age of 8¾ years, observation showed an increase in weight to 39 pounds (17.7 Kg.) and in height to 43 inches (109.22 cm.). The genu valgum had disappeared, and the physical outline was nearly normal. A brother 1 year younger was 6 inches (15.24 cm.) taller, however. The teeth were good. The child was active and attended school regularly. Roentgen examination showed disappearance of the former rickets and osteoporosis. Strict control of the diet in regard to the content of fat continued. Administration of ultraviolet radiation regularly twice a week and 1 tablet of irradiated ergosterol daily was continued.

The final observation made in 1933 revealed the continued satisfactory course. The patient was well developed with little prominence of the abdomen. He was somewhat small, however, but was active and strong and very bright. No deformity remained. Determinations of the metabolism of fat revealed, however, that

(with the fat-restricted diet) 3.75 Gm. of fat were still excreted daily. The dietetic and medicinal regimen for the treatment of celiac disease was continued.

CASE 12.—O. A., a girl, was admitted to the hospital in February 1925 with the typical clinical picture of celiac disease. A photograph is shown of her condition at that time (fig. 11 *A*). At the age of 2 years her weight was only 15 pounds (6.8 Kg.) and her height 27 inches (99.06 cm.).

In September 1925 rigid dietetic control was instituted with a diet high in protein, consisting of defatted milk, casein, lean meat of chicken, egg and small amounts of ripe banana. A month later the daily administration of irradiated ergosterol was commenced.

In February 1926 there was marked improvement in the general condition, with gain in weight. This was progressive, except a relapse of a few weeks in October (apparently associated with whooping cough), and by the middle of

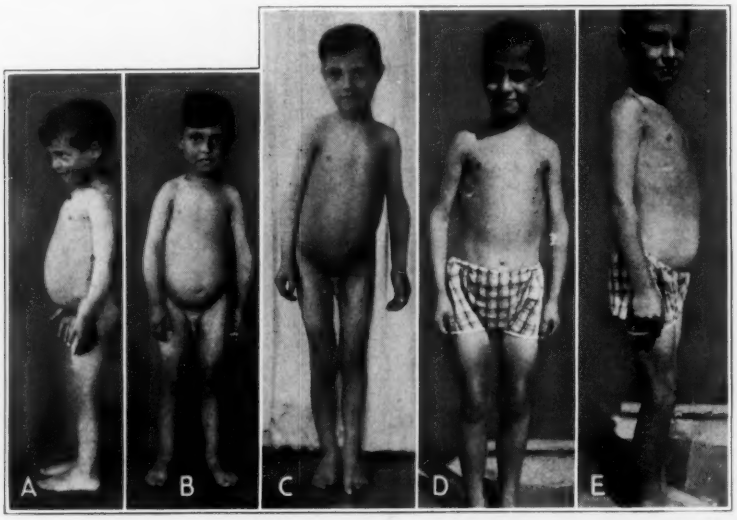

Fig. 10 (case 11).—Series of photographs of G. P. *A* and *B* were taken in 1928, after about two years of treatment; *C*, in 1930, and *D* and *E*, in 1933, at the age of 11½.

December 1926 the child was able to walk well. In the meantime, she had grown 4 inches (10.16 cm.) in height, and her weight had increased to nearly 21 pounds (9.5 Kg.). She had become happy and alert. Roentgenographic examination of the long bones showed osteoporotic structure, but no evidence of rickets was detected.

Throughout the period between 1925 and 1928 the child had been under continued medical supervision (in a hospital or home for convalescent patients) and had received a diet free from fats and small doses of irradiated ergosterol daily. In the warm summer days she had been allowed to be outdoors in the sunshine with little clothing. Careful restudy of the patient in August 1928 showed that the general condition was excellent. The physique was good. She was of normal mental development. The teeth were good. The bones were normal except a degree of osteoporosis. The musculature was good. The abdomen was still

moderately prominent. When the child was given the regulated diet there was one normal-colored, formed stool daily. Brief experimental feeding of a full varied diet resulted in an increased number of stools and biochemical evidence of persistent intolerance for fats. The weight had now reached 33 pounds (15 Kg.), and there had been a total gain in height of nearly 10 inches (25.4 cm.) since treatment was commenced.

A comment in 1928 stated: "This is a severe case of celiac disease in which good progress has been made under dietetic control. The administration of irradiated ergosterol has allowed more adequate growth without the supervision of rachitic changes in the bones. Biochemical examinations show that even after prolonged intestinal rest from the use of fats there is evidence of incapacity to deal adequately with them. It is remarkable that this child is now only 6 inches (15.24 cm.) shorter and 4 pounds (1.8 Kg.) lighter than the average child of her age."

TABLE 12.—*Summary of Data in Case 11*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
July 1923	2	.....	....	....	....	....	....	....	...	..	..	
March 1926	5	Ordinary	40.0	24.0	16.2	11.0	12.0	....	...	..	20	Hospital treatment commenced; rickets treatment commenced
July 1928	7½	Free from fats	32.3	14.5	17.7	11.0	5.2	10.9	5.0	38	31	
Nov. 1930	8¾	Free from fats	....	....	....	....	....	....	...	43	39	Bones normal
Aug. 1933	11½	Free from fats	25.9	17.7	8.2	14.2	3.5	9.5	3.2	..	..	
Aug. 1933	11½	Free from fats	Daily output of fat, 3.75 Gm.					....	...	47	49	Physique good

In 1931 detailed observations were again made, and it was noted that good dietetic control was being maintained and irradiated ergosterol supplied daily. Ultraviolet irradiation had been discontinued in February 1929. The slightest "cold" used to produce diarrhea, but this was no longer so. The hair was growing more rapidly and was thicker. The physique was good, but the child was short. The muscular development was improving. The gluteal muscles were becoming normal. The sclerotics were still slightly blue. The bones showed only slight osteoporosis. It was observed that any increase of fat in the diet precipitated an attack of diarrhea with stools of the type seen in celiac disease.

In 1933, at the age of 11, the girl had been under observation and treatment for about nine years. The clinical results showed ample justification for the continued supervision. She was a well built girl of good posture and mentality. There was no physical deformity. The teeth were good. Growth had been rapid during the preceding two years. The sclerotics were white and clear. Puberty had not yet been reached. The use of the restricted intake of fat was continued,

and she received irradiated ergosterol daily. The mother said the child had improved "remarkably during the past few years." It is to be noted that this child had been under continued observation, and during the entire time rickets had not developed. The appearance of the bones had been consistently satisfactory, except osteoporosis in the earlier years. No deformity of the bones had occurred, and in 1933 the skeleton was excellent. A note at this time advises careful continuation of the regimen then practiced so long as intolerance to fat was shown.

CASE 13.—M. C., a girl, was the first child of a family of three children, the others of whom were well. She never had been breast fed.

The patient was first observed in October 1926, at the age of 4 years. There was a history of "always having been small and pale, with a prominent abdomen, large greasy, offensive stools and occasional vomiting."

Fig. 11 (case 12).—Series of photographs of O. A. *A* was taken in February 1925; *B* and *C*, in 1928; *D*, in 1929, and *E* and *F*, in 1933, at the age of 11.

The child presented a typical picture of celiac disease. Biochemical analysis of the stools confirmed the diagnosis. A roentgenogram showed a deficiency of calcium in the structure of the bones but no rickets. The weight was only 17½ pounds (7.9 Kg.). In the hospital at the time of admission the diet was regulated on the basis of the usual principles for this condition. Ultraviolet radiation and irradiated ergosterol in small daily doses were also given. This regimen was carefully followed for the next nine months, and during this time splendid progress was made in the general state. The child grew well and had no rickets. After her discharge for control of the treatment in the outpatient department, the parents failed to continue the recommended treatment or to bring the child to the hospital for observation.

In July 1928 she was sought and it was found that her condition was deteriorating. Diarrhea, with passage of stools typical of those associated with celiac

disease, had recurred. The abdomen was prominent. The teeth were moderately good. No abnormality of the viscera was found. The general state of the child was poor. She had made a net gain of only 4 pounds (1.8 Kg.) in the two years since first attending the hospital. Roentgenograms then showed rachitic changes

TABLE 13.—*Summary of Data in Case 12*

Date	Age, Yr.	Diet	Analysis of Stools: Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Analysis of Blood: Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
Feb. 1925	2	Varied	60.8	....	....	....	....	....	...	27	15	On admission
Feb. 1925	2	Fat-free	14.2	1.9	12.3	1.2	0.7	....	...	..	..	
March 1925	2	Fat-free	13.7	2.9	10.8	2.9	0.0	....	...	..	..	Improvement
March 1925	2	Fat-free	8.1	1.3	6.8	....	....	....	...	..	..	
Sept. 1925	2½	Varied (trial)	42.3	....	....	....	....	6.8	3.3	..	..	Irradiated ergosterol
Dec. 1925	2¾	Varied	36.0	17.3	18.6	14.7	2.6	....	...	..	..	Ultraviolet irradiation commenced
June 1926	3¼	Fat-free	19.6	5.8	13.7	3.1	2.8	....	...	30	20	
Oct. 1926	3½	Fat-free	....	....	....	....	....	10.5	4.8	..	..	
Jan. 1927	3¾	Fat-free	16.0	3.5	12.5	0.2	3.3	11.9	4.4	31½	22	Excellent progress
March 1928	5	Moderate amount of fat	24.0	5.5	18.5	4.5	0.9	....	...	..	..	Irradiated ergosterol
April 1928	5	Varied (trial)	32.0	14.9	16.9	12.3	2.6	....	...	..	..	Experimental diet
April 1928	5	Varied (trial)	33.0	6.4	26.4	4.0	2.3	....	...	..	..	Experimental diet
Aug. 1928	5½	Fat-free	....	....	....	....	....	....	...	37	36½	
1931	8	Fat-free	Two stools daily, small and pale					....	...	45	44½	Irradiated ergosterol three times daily; diarrhea produced by any increase of fat; bones normal
1933	11	Restricted fat	25.0	13.5	12.0	6.0	7.5	9.2	3.8	51	56	Irradiated ergosterol regularly
Excretion of fat in stools still about 6 Gm. daily												
Average normal values.....										53	66	

in the epiphyses and genu valgum had developed. It was evident, therefore, that the patient had suffered adversely as a result of parental slackness. She was readmitted for careful control of the condition. In August, one month later, return of the former good progress was attained; the general condition became immensely improved; the stools were normal, and the condition of the bones showed rapid response, as indicated by the healing of the rickets. Two months after recommencement of treatment the rickets had completely healed.

A comment in 1928 stated: "This is a case of celiac disease in which good response to treatment was obtained at the age of 4 years. Relaxation of dietetic control and other treatment by the parents caused marked deterioration, with occurrence of rickets and retardation of general development. Reestablishment of dietary control and auxiliary vitamin D therapy resulted in rapid and maintained response. Marked intolerance for fats was detectable at the age of 6." The increase and decrease in the calcium content of the serum, synchronous with the progress and relapse, are shown in the table.

During the winter of 1929 while the child was at home, further relaxation of the dietetic control and the administration of medicinal vitamin D occurred.

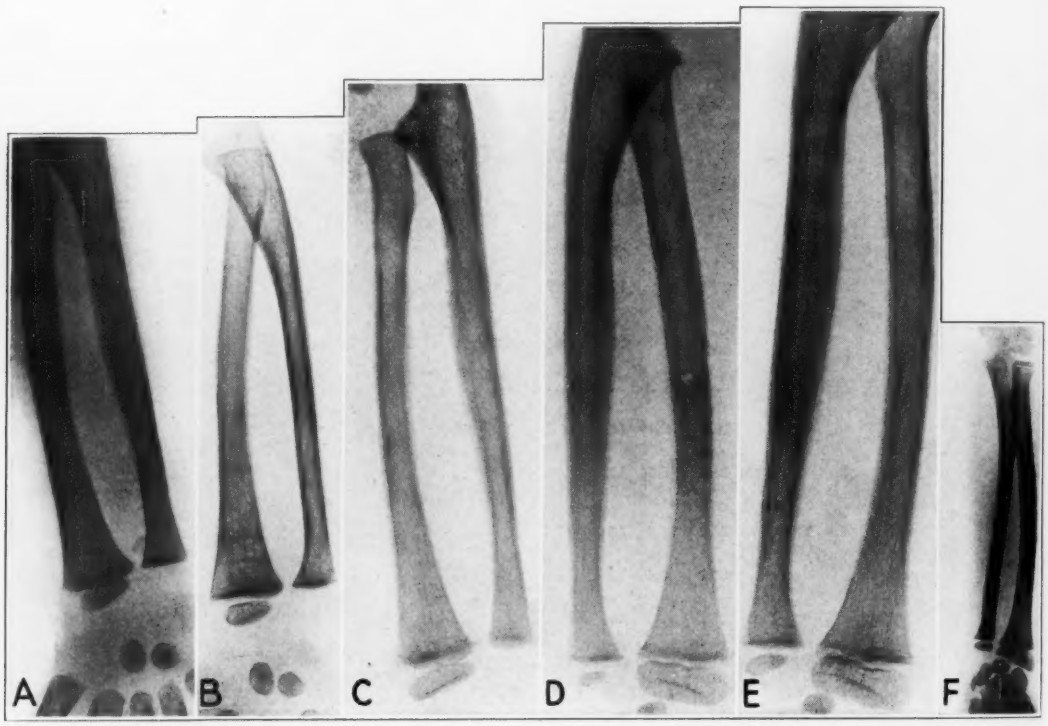

Fig. 12 (case 12).—Series of roentgenograms of the forearm. *A* was taken on Oct. 31, 1926; *B*, Feb. 14, 1927; *C*, April 14, 1928; *D*, Nov. 18, 1929; *E*, Dec. 17, 1930, and *F*, Sept. 7, 1933.

Symptoms reappeared, and a further development of osteoporosis and epiphyseal changes (rickets) was detected. After this, however, improved cooperation of the parents was obtained, with the result that detailed examination of the child in 1931 revealed satisfactory progress. Administration of a diet free from fats was continued, and irradiated ergosterol was given daily. The child attended school regularly and was active. The gluteal muscles were developing normally, and the abdomen was less prominent. The hair was growing better (a good index of progress). There was no diarrhea, and the stools were much improved.

Intermittent observations were continued, and the following report indicates the situation in July 1933, seven years after the girl first came for treatment.

The physique was fairly good. The patient was straight and slender. The chest was well formed. The teeth were good. Growth was satisfactory. There were no signs of deformity. The sclerotics were of normal color. Puberty had

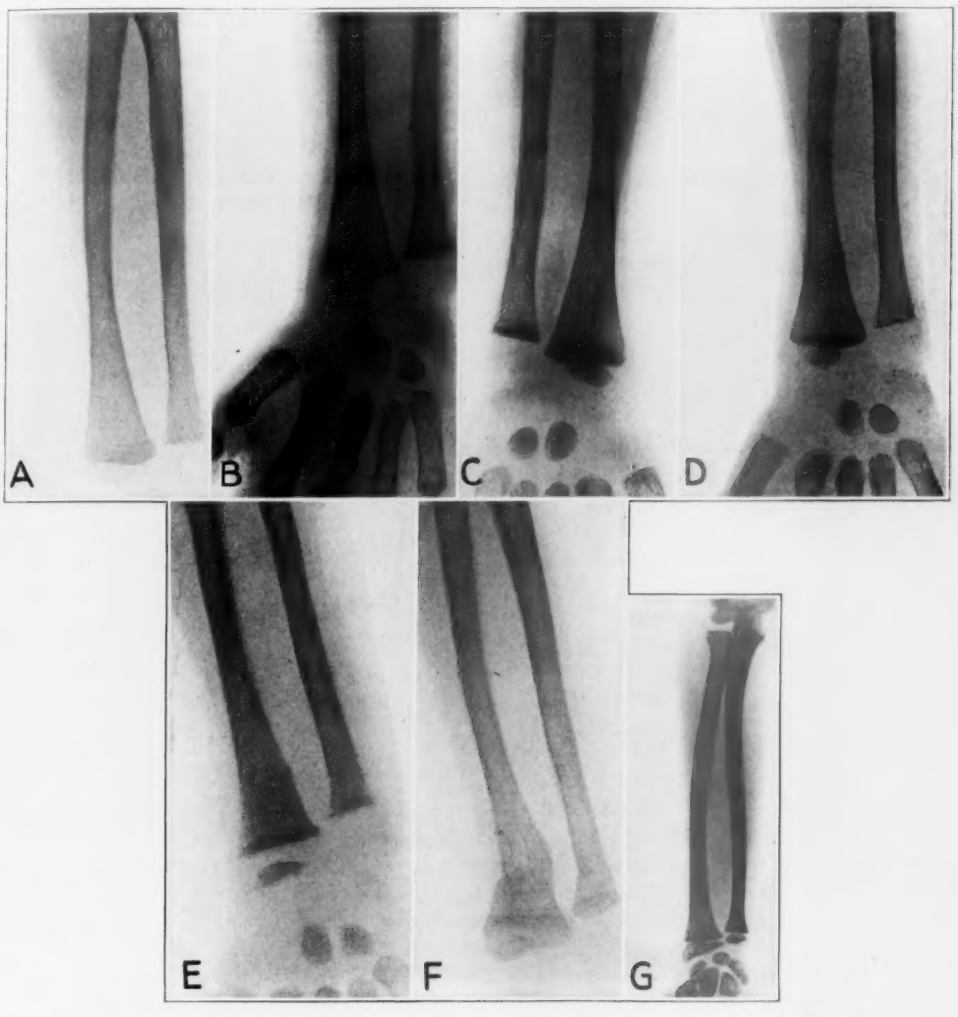

Fig. 13 (case 13).—Series of roentgenograms of the forearm of M. C. *A* was taken on May 4, 1927; *B*, Aug. 29, 1928; *C*, Sept. 10, 1928; *D*, Jan. 3, 1929; *E*, March 11, 1929; *F*, April 18, 1929, showing relapse, and *G*, July 27, 1933.

not yet been reached. The height and weight were good. The child was receiving practically a full varied diet, including butter and ordinary milk but no other fats. The stools were of normal consistency, color, etc. The bones were normal, clinically and roentgenographically. The child had had no intercurrent infection.

Case 14.—D. S., a girl, was the third child of a family of four children, all the others of whom were healthy. The patient was breast fed for one year; she then received cow's milk and a varied diet.

When first observed in May 1926, at the age of 3½ years, she was poorly developed and undersized. Intestinal trouble had commenced two years previously when cow's milk and "ordinary" food were first given. Diarrhea and large stools were present. There was no growth or gain in weight. Malt and cod liver oil had been given, which made the diarrhea worse. The abdomen was full. There was no fever. The weight was 19½ pounds (8.85 Kg.). Roentgenograms revealed structure of the bones characteristic of celiac disease. There was no rickets.

In May 1927 the child was given a diet consisting of rusk, bread, honey, ham, lean meat, sweet fruit and skimmed milk; ultraviolet radiation was administered for five months and then 1 tablet of irradiated ergosterol twice a day.

Table 14.—*Summary of Data in Case 13*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
10/18/26	4	Varied	42	32.0	10.5	17.3	14	9.0	5.6	..	..	Admission
1/ 5/27	4¼	Free from fats	9	2.5	6.5	0.5	2	11.6	4.5	..	17½	Regular treatment in hospital irradiated ergosterol
7/ 7/28	5¾	Varied	59	38.0	20.5	27.0	10	8.4	4.7	33¾	22	Relapse
Dec. 1931	8	Free from fats	One stool daily					....	...	43½	42	Strict control maintained
July 1933	10¾	Ordinary restricted	Normal appearance					9.8	3.5	51½	54	See fig. 14 C and D
Average normal values.....										52	56	

In August 1928 the diet and the administration of irradiated ergosterol were still maintained. The general health was good. The child attended school regularly and was mentally bright. Growth was perceptible, more especially during the preceding year. The hair also grew well (until eighteen months before it was very scanty and fine). The stools appeared normal (when the child had a fat-free diet). No rachitic signs or deformities were present. The teeth were excellent and all were present. The eyes were normal. Examination of the chest elicited normal signs. The spleen and liver were not palpable. The gluteal muscles were of average development. The abdomen was normal in contour. The urine was normal. Roentgenograms of the bones showed atrophic structure characteristic of celiac disease but no rickets. The height was 40 inches (101.6 cm.) and the weight 33½ pounds (15.2 Kg.). The abdomen measured 17½ inches (44.45 cm.).

In 1933, at the age of 10, the weight was 60 pounds (27.2 Kg.) and the height 54½ inches (138.4 cm.). There were no abnormal clinical signs. The child had been given an ordinary diet for about a year. The stools appeared normal The physique was good.

CASE 15.—D. S., a girl, was the second child of a family of three children, the others of whom were normal. The child was breast fed for ten months, and she then received a varied diet.

In September 1926, at the age of 3 years the child had been in poor health for several months. She was languid and was losing weight. There were three stools a day, which were bulky, greasy and offensive. The child was moderately well nourished. The abdomen was full. The liver and spleen were not palpable. The heart and lungs were normal. The stools were pale and typical of those associated with celiac disease. The weight was 25 pounds (11.3 Kg.).

Observation was made in August 1928, when the child was 5. Since her discharge from the hospital in September 1926 she had been on a diet restricted in

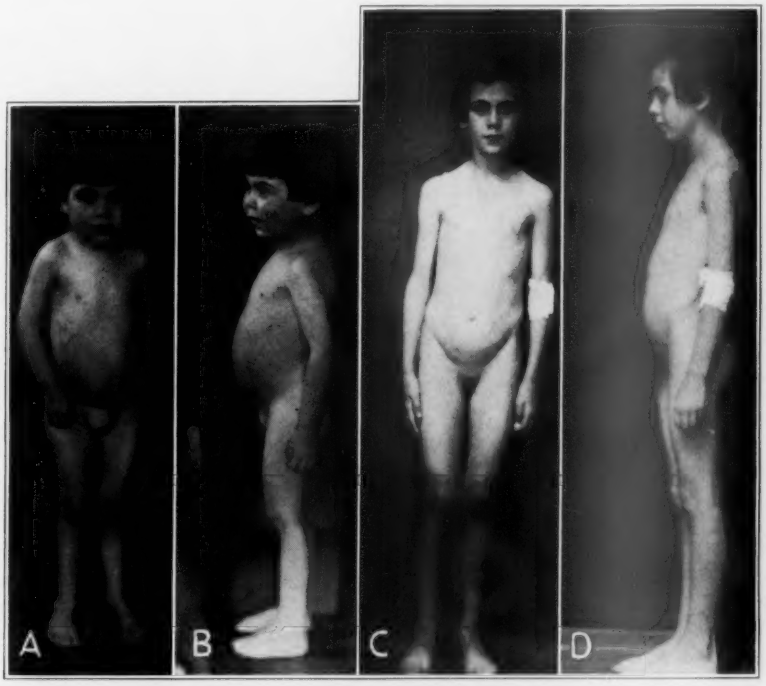

Fig. 14 (case 13).—Series of photographs of M. C. *A* and *B* were taken in 1928, and *C* and *D*, in 1933 at the age of 11.

fats. No ultraviolet radiation or drugs had been given, but she was kept in the sunshine a good deal in a rural district. She was apparently growing more rapidly. The general health was fairly good. There were two movements of the bowels a day, with pale feces; the child had returned to a somewhat varied diet for several months. Slight upsets, such as a "cold" caused an increase in the number of stools and resulted in a looser consistency. No deformities or signs of rickets were noted. There was no tetany. The teeth were good, and all of them were present. The sclerotics were normal. The abdomen was of more normal appearance, but it was still prominent. The gluteal muscles were poorly formed. The liver and spleen were not palpable. The heart and lungs were normal. There was no fever. The height was 40 inches (101.6 cm.) and the weight 32 pounds

(14.5 Kg.). The abdomen measured 16½ inches (41.9 cm.). Roentgenograms revealed slight osteoporosis. There was no rickets.

Examination in November 1930 revealed that the restriction of fats in the diet had been better controlled since 1928. Slight genu valgum was still seen, but the physique was much improved. No diarrhea was present. The stools usually appeared normal. The hair was growing well. The teeth were good. The gain

TABLE 15.—*Summary of Data in Case 14*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
Oct. 1927	4	Varied	35	17.4	16.9	12.6	4.8	....	...	..	20	Typical celiac disease
Aug. 1928	5	Free from fats	11	5.2	5.7	3.6	1.7	11.2	6.3	40	31	After strict treatment
Sept. 1933	10	Varied	18	6.4	12.0	3.7	2.7	10.5	4.3	55	60	Appearance good

TABLE 16.—*Summary of Data in Case 15*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
Sept. 1926	3	Varied	37	20.6	15.6	11.4	9.0	....	...	..	25	Poor general condition
Aug. 1928	5	Restricted in fats	28	7.9	20.0	6.3	1.3	12.6	5	40	32	
Nov. 1930	7½	Restricted in fats	Stools satisfactory in appearance; occasional looseness					....	...	45	45	Growth good
Aug. 1933	10	Varied	30.7	17.1	13.6	15.4	1.7	8.4	4	55½	59	Decrease in blood calcium content; no special vitamin supply
			Daily excretion of fat when varied diet is given, 3.7 Gm.									

in weight was 13 pounds (5.9 Kg.), and the increase in height 5 inches (12.7 cm.) in two years. Roentgenograms confirmed the normal structure of the bones.

In 1933, at the age of 10, examination showed a good general outline of the body, loss of abdominal prominence, good general muscular development and no deformities. The patient had reached a height of 55½ inches (140.97 cm.) and weighed 60 pounds (27.2 Kg.); the abdomen measured 22 inches (96.36 cm.) and the chest 24 inches (91.44 cm.). The hair was normal. The teeth were good. The mental development was excellent, and the patient attended school regularly. There was still, however, intolerance for fats. The fat content of the diet had to remain within very restricted limits; otherwise, especially if the child had a slight

infection, such as a cold, loose stools occurred. A test for fat metabolism when she was given a varied diet revealed excretion of 3.7 Gm. daily. Continued supervision was therefore indicated. The roentgenogram of the bones was normal. Vitamin D and ultraviolet radiation had never been prescribed.

CASE 16.—R. C., a boy, was the eighth of a family of eight children, all the rest of whom were healthy. He was never breast fed but was given whole cow's milk in infancy.

The progress of this child was apparently normal until he was 2 years of age. He then began to have attacks of diarrhea with pale stools, and abdominal distention developed.

On admission to the hospital in October 1927, at the age of 3, he was subnormal in size and weight. The stools were typical of those seen in celiac disease, and biochemical examination showed a large content of fat. There were no clinical or roentgenographic signs of rickets, but osteoporotic structure of the

TABLE 17.—*Summary of Data in Case 16*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
Oct. 1927	3	Varied	48.0	37.3	10.6	27.4	9.9	10.0	4.0	..	..	
Aug. 1928	4	Free from fats	12.6	4.9	7.7	3.0	1.8	10.6	4.7	25	29	Careful control
1930	6	Free from fats	No diarrhea					....	...	42	37	
1933	9	Varied	Normal					9.2	3.0	47	48	Clinically normal

bones was shown. For the following two months the child's diet was not modified, and progressive loss in weight occurred.

In January 1928 a regimen for the relief of celiac disease was commenced with rigid dietetic control. One tablet of irradiated ergosterol was given daily. Within a short time improvement commenced, and in August 1928 the general health had improved remarkably. The child was growing slowly. The stools were satisfactory, and the abdomen was considerably smaller. At the age of 3¾ years, he had reached 35½ inches (90.17 cm.) in height and weighed 29 pounds (13.2 Kg.).

A comment in 1928 stated: "This is a case of moderately severe celiac disease in which good response to early and continued treatment was obtained."

In 1930 the physique was further improved. Dietetic control was maintained; no diarrhea was present.

In 1933, at the age of 9, the child was given a full diet, and no clinical abnormality was present.

CASE 17.—L. P., a girl, was the third child of a family of four children. She had been breast fed for six weeks, after which she received whole cow's milk.

Symptoms were definitely observed in this child at the age of about 1 year. Her weight failed to increase; she remained puny, and troublesome diarrhea with occasional vomiting developed.

On admission to the hospital in September 1927 at the age of 2½, she was thin and wasted and weighed only 15½ pounds (7.02 Kg.). She appeared ill and irresponsive. The abdomen was enlarged and soft, and the gluteal region was wasted. The stools were light in color and were porridge-like and fetid. There were no signs of rickets, but the bones were atrophic in roentgenographic appearance. Biochemically, the stools were exceedingly fatty (of the type seen in celiac disease).

Treatment was commenced immediately and followed the usual dietetic lines; ultraviolet radiation was given three times weekly. Progress was satisfactory, and in twelve months the child had gained 11½ pounds (5.2 Kg.) and had reached 31 inches (78.74 cm.) in height. The general condition was much improved, and the abdomen was smaller. There was one stool a day when the child was given a diet free from fats. The nature of the stools when the patient received a varied diet somewhat restricted in fats showed that the tolerance for fats had greatly improved.

TABLE 18.—*Summary of Data in Case 17*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
Sept. 1927	2½	Varied	75	28.8	46.0	20.5	8	....	...	..	15½	Admission
Aug. 1928	3½	Restriction in fats (trial)	23	10.6	12.5	5.7	5	....	...	31	27	Good progress; strict dietary control
Dec. 1930	5½	Mixed	Stools fatty when control of diet was relaxed					....	...	40½	41	Diet not adequately controlled
Aug. 1933	8	Free from fats	8.2	7.2	1.0	4.2	3.0	9	6	47	54	Good growth and physique
			1.5 Gm. of fat excreted daily									

A comment in 1928 stated: "This is a case of an early stage of celiac disease in which there are an excellent response to treatment and rapid improvement in the tolerance for fats. The patient is now 3½ years old and is developing well, although she is 6 inches (15.24 cm.) less than the average height."

In December 1930, at the age of 5½ fairly good progress was maintained. The child weighed 41 pounds (18.6 Kg.) and had grown nearly 10 inches (25.4 cm.) since 1928. The abdomen was still prominent; the gluteal muscles were poorly developed, and the general muscular strength was only moderate. Slight genu valgum and roentgenographic evidence of slight osteoporosis were present. There was no rickets. The teeth were good. The hair was thick. The diet had been allowed to contain more fat than is usually recommended, with the result that at intervals the stools were unformed, pale and fatty. The mother of this child had to go out to work, and hence the home supervision was not first class. The dietary regimen was reestablished, and instructions were given.

A further examination in 1933, when the girl had reached the age of 8, showed satisfactory results. A further increase of 6 inches (15.24 cm.) in height and a gain in weight to 54 pounds (24.5 Kg.) were noted. No deformity was present.

The stools were satisfactory. The physique was good, and the child was well built. The musculature was well developed.

CASE 18.—E. L., a girl, was the only child. She had been breast fed for six months, after which she was given cow's milk.

The patient first came under observation in November 1927 at the age of 2 years. She had been "delicate" ever since she had been weaned, when troublesome diarrhea developed, with large, offensive stools, sometimes five a day. There were progressive loss of weight and occasional vomiting. The abdomen was enlarged. The weight was only 17 pounds (7.7 Kg.). Clinical and biochemical features were typical of those associated with celiac disease. Dietetic treatment with defatted milk and added casein was instituted immediately, and within three weeks there was definite improvement; the child became more responsive and pleasant, and there was a slight gain in weight. The long bones showed the usual osteoporotic state but no rickets.

TABLE 19.—*Summary of Data in Case 18*

			Analysis of Stools					Analysis of Blood				
Date	Age, Yr.	Diet	Total Fat	Unsaponified Fat	Saponified Fat	Free Fatty Acid	Neutral Fat	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Height, In.	Weight, Lb.	Comment
Dec. 1927	2	Varied	52	32.0	20.0	20	11.0	....	...	..	17	Poor general condition
Aug. 1928	2¾	.....	..	....	....	..	....	10.7	4.5	..	..	Irradiated ergosterol
Aug. 1928	2¾	Varied (trial)	37	11.6	25.4	9	2.5	....	...	33	22	Good progress; much improvement
Dec. 1930	5½	Free from fats	Normal appearance of stools					....	...	39	36	Physical development not complete
Aug. 1933	7	Varied	27	12.4	14.8	9.6	2.8	9.5	3.6	44	42	Recovery not yet complete
			Excretion of 3 Gm. of fat daily									

During the following nine months regulation of the qualitative and quantitative nature of the diet was strictly adhered to, with correspondingly good results. Irradiated ergosterol was given daily. The bowel movements became normal, with formed stools (when the diet was controlled). The teeth were good. The musculature was moderately developed. No abnormality of the viscera was found. There was no evidence of rickets, but osteoporosis was still present. When the child was temporarily given a full diet, the feces again became of the type associated with celiac disease.

The weight was 22 pounds (10 Kg.) and the height 33 inches (83.82 cm.); the circumference of the abdomen was 17½ inches (74.93 cm.) at the level of the umbilicus.

In 1930, at the age of 5, the careful dietary had been closely followed. Two tablets daily of irradiated ergosterol and occasional courses of ultraviolet radiation had been given. The outline of the body was improved, and a growth of 6 inches (15.24 cm.) and a gain of 14 pounds (6.4 Kg.) had occurred. The musculature was improved. There was one stool daily. The hair had grown much better recently. The bones had become normal. The teeth were good.

The examination in 1933, at the age of 7, showed that during the past year the child had taken an ordinary mixed diet with simple restriction of fat with no untoward result. The physique was nearly normal. The stools appeared normal, but on analysis excess of fat was still shown. It was calculated that 3 Gm. of fat was excreted daily.

The child had shown good general development since the commencement of treatment. She was bright and alert. She was able to start school at the age of 5. The celiac disorder was controlled, but the level for the excretion of fats was not within normal limits. Continuation of supervision was advised.

COMMENT

A review of the foregoing cases of the celiac disorder reveals how satisfactory the final results may be when cooperative and long continued treatment and supervision of the patients are maintained. The most important therapeutic measure is, of course, dietetic control, and except in some cases of the more severe type, attention to this alone is almost sufficient to insure satisfactory progress. In such cases omission from the diet of fat-containing foods is usual. It is essential in most cases to add vitamin concentrates daily. In the majority of the cases which we have reviewed, the patient was given a preparation of vitamin D by mouth (usually irradiated ergosterol), and in many instances irradiation of the skin was employed. The effect of intensive vitamin D therapy in the cure of tetany and in the rapid healing of rickets and restoration of the normal structure of the bones in the cases in which osteoporosis is shown is clearly demonstrated. In the cases in which deformity of the bones was shown initially, continued treatment insured disappearance of curvature of the limbs; this is especially apparent in cases 3, 4 and 9. Even the advanced deformity present in case 2 showed improvement during the period of adequate treatment, only to increase, however, when treatment was discontinued and rickets and severe osteoporosis reappeared.

With the exception of the patient in case 2, who had been taking a yeast preparation regularly, these children were not given other vitamin concentrates during the more active phases of the disorder, and the records of the cases here reviewed have not demonstrated any obvious deficiency diseases which might have resulted from this omission. Frank scurvy is a rare complication of celiac disease, as is also the megalocytic hyperchromic anemia, which Vaughan attributed to the lack of some portion of the vitamin B complex.

Pellagrinoid conditions of the skin, eczema and other cutaneous disorders have been described in cases of celiac disease, especially those in adults, and we have observed these changes in patients who have recently come under supervision at this hospital. Such cases, however, have not been noted in the present series, and atrophic changes in the skin and

hair which were present at the first examination rapidly disappeared with dietetic control of the essential steatorrhea. Xerophthalmia has not been observed in our series of cases; nevertheless, in the present state of knowledge of the vitamins and the effects of the lesser degrees of hypovitaminosis A, B and C, and in view of the occasional occurrence of these deficiencies in cases of severe and neglected celiac disorder, it would appear advisable to add to the diet, besides the essential vitamin D, other vitamin concentrates, such as carotene (vitamin A), Marmite (vitamin B) and orange juice (vitamin C). This has been our practice in the treatment of patients with the more active forms of the condition who have come under our care during the past five years.

Clinical and biochemical grades of severity of steatorrhea will be observed in the reports of the cases, but, exclusive of case 2, in no instance had the disease been so severe or prolonged as to allow severe permanent disability or deformity. In several cases rickets was present, and in nearly all instances osteoporosis was detectable roentgenographically. However, adequate recovery from these secondary effects was soon obtained with suitable treatment. The muscular system reveals interesting clinical features of the celiac disorder, namely, the characteristic atrophy of the gluteal and thigh muscles and weakness of the abdominal muscles, which leads to prominence of the abdomen and gives the patient a peculiar characteristic physical outline, to which attention was first directed by Miller. Return to the more normal outline of the body is a feature of satisfactory progress in recovery from the disease, and although slow, it can be confidently anticipated, so that with efficient control a normal appearance is one of the rewards of years of patient dieting.

It has been observed that periods of slow and of more rapid improvement in the general symptoms and signs occur. In the cases of fairly severe disease many months may pass with slow gain in weight and little increase in height, after which, however, a period of more rapid gain occurs. In some cases the clinical progress is remarkably accelerated after an apparent standstill of months' duration, but the urge to growth which occurs at puberty is frequently striking. Rapid fluctuations in weight are not uncommon during the more severe phases of the disorder, and these are to some extent concerned with the peculiar instability of the tissues in regard to their fluid content (hydrolability)—clinical dehydration and slight edema appearing and disappearing without much noticeable change in the general state of the patient. As good progress takes place, however, a continued increase in weight due to actual growth of tissue is usual.

TABLE 20.—*Data on Features Relating to the Physical State of the Patients*

No.	Patient	Sex	Age at Onset of Disease, Yr.	Age at Commencement of Treatment, Yr.	Age in 1933	Height, In.		Weight, Lbs.		Normal Weight for Height, Lb.	Weight in Relation to the Average Normal for the Actual Height, Lb.	Weight in Relation to the Average Normal for the Actual Age, Lb.	Height in Relation to the Average Normal for the Actual Age, In.
						Actual	Normal	Actual	Normal				
1	L. H.	F	1	15	23	60	63	95	120	98	— 3	—25	— 3
2	R. D.	M	3	10½	18	45	67	66	136	47	+19	—70	—22
3	D. D.	F	2	7¾	18½	57	62	114	120	86	+28	— 6	— 5
4	M. R.	F	4	5	18	60	62	126	120	96	+32	+ 6	— 2
5	M. G.	F	1¼	4	16	63½	61½	104	113	120	—16	— 9	+ 2
6	H. B.	F	4	6½	15	63	61	109	106	120	—11	+ 3	+ 2
7	S. P.	F	2	10½	14	52½	59½	68	101	68	same	—33	— 7
8	L. M.	F	2	3	13	53	57	63	87	68	— 5	—24	— 4
9	J. B.	F	1½	7	13	49	57	54	84	56	— 2	—30	— 8
10	A. R.	M	2	5	12	45	55½	47	76	48	— 1	—29	—10
11	G. P.	M	2	5	11½	47	54	49	68	55	— 6	—19	— 7
12	O. A.	F	1	2	11	51	53	56	66	58	— 2	—10	— 2
13	M. C.	F	2	4	10½	51½	52	54	56	60	— 6	— 2	— ½
14	D. S.	F	1	3½	10	54½	51	60	62	68	— 8	— 2	+ 3½
15	D. SEE	F	2	3	10	55	51	59	62	72	—13	— 3	+ 4
16	R. C.	M	2	3	9	47	50	54	60	56	— 2	— 6	— 3
17	L. P.	F	1	2½	8	47	46½	54	52	52	+ 2	+ 2	+ ½
18	E. L.	F	1	2	7	44	44	42	47	47	— 5	— 5	Same

Determinations of the actual height in regard to the age at the time of examination revealed dwarfing in ten cases, ranging from 2 to 10 inches (5.08 to 25.4 cm.). In four cases the height was greater than the average normal value for a person of the age of the patient, and in three instances the height may be regarded as being of the average normal value. When weight is considered in association with height, in two cases the weight was 28 and 32 pounds (12.7 and 14.5 Kg.), respectively, more than the normal; in eleven cases it was within 10 pounds (4.5 Kg.) of the average value, and in only three instances was it more than 10 pounds below the average weight for a person of the actual height of the patient. The height of the three persons last mentioned was somewhat greater than the average normal value. A more reasonable comparison is that of the weight and the actual height of the patient; for instance, the height of H. B. (case 6) was 2 inches (5.08 cm.) above the average, although the weight was 11 pounds (5 Kg.) below the average normal value. The weight was 3 pounds (1.3 Kg.) above normal as compared with that of a girl of her actual age. The reverse is shown, however, in case 3 (D. B.). It is not uncommon for a child with celiac disease to gain weight rapidly as good progress occurs (usually after a few years' treatment) and at one phase of the course of medication to show a tendency to actual obesity, that is, a weight disproportionate to the height. This phenomenon was best observed in case 4 (M. R.) in this series; the subcutaneous fat became so evident as to give a physical outline not unlike that observed in cases of Fröhlich's syndrome. Later, however, and quite spontaneously, adjustment occurred, so that the final weight (at the age of 18) was only 6 pounds (2.7 Kg.) above the normal weight for a person of her actual age, but it was still 32 pounds (14.5 Kg.) above the usual weight for a person of her height, the patient being 2 inches (5.08 cm.) shorter than normal. Similar facts are indicated in case 3 (D. B.).

To summarize, however, most patients were observed to be approximately of the average weight for their height. Three weighed only 10 pounds (4.5 Kg.) or more less than the average in this respect. A fairly well balanced ratio of height to weight is, therefore, usual for the patient who finally reaches the phase of established recovery after, in most cases, prolonged remedial therapy.

Anemia.—Ever since the first and classic description by Gee,[2] celiac disease has been recognized as a disorder frequently associated with pallor and anemia. Herter [5] referred to the anemia present in all the five cases forming the basis of his study, which from his description appears to have been of the hypochromic type. The anemia of the celiac

5. Herter, C. A.: On Infantilism from Chronic Intestinal Infection, New York, The Macmillan Company, 1908.

disorder received careful and exhaustive consideration by Bennett, Hunter and Vaughan.[1] With one possible exception, in all the cases studied by these authors symptoms of the celiac disorder had developed during childhood, but the disease had remained unrecognized and untreated until adult life was reached. In twelve of their fifteen cases hematologic examination was made; in three of these the findings were normal, and in nine anemia was shown, which was described as being of three types:

1. Hypochromic anemia with anisocytosis and microcytosis. This type responds well to treatment with iron but not with Marmite. It was present in five cases.

2. Megalocytic hyperchromic anemia. From a perusal of the literature and in our own experience, this type is much rarer than the hypochromic forms. This type was present in two cases in the series cited, and in both cure was effected with large doses of Marmite.

3. Erythroblastic anemia, that is, anemia characterized by the appearance in the blood stream of nucleated red cells and immature white cells of the myeloid series—a hematologic picture rather than a clinical entity. This blood picture was present in the two remaining cases studied by these authors and responded well to treatment with massive doses of iron, though immature cells were still present after the anemia had disappeared.

In our series of eighteen cases of celiac disease recognized during childhood and supervised over many years, sixteen patients have been examined hematologically. In this examination attention was focused on the red cells, but films prepared with the Leishman stain failed to reveal evidence of the leuko-erythroblastic blood picture already mentioned.

Technic.—Blood was obtained by pricking a finger with a Frank needle. The red cells were enumerated in a Bürker counting chamber. Both sides of the chamber were filled after the pipet had been shaken for three minutes, and three columns, each 3 mm. in length, were counted on each side; counts showing a difference between the two sides of more than 20 cells were discarded. Normal values for the red cell count are from 5,100,000 to 6,350,000 per cubic millimeter for men and from 3,940,000 to 6,080,000 for women (Price-Jones[6]).

Estimations of hemoglobin were made with a Haldane hemoglobinometer supplied by Hawksley & Son and checked by them at frequent intervals. One hundred per cent according to this standard is equivalent to 13.8 Gm. of hemoglobin per hundred cubic centimeters of blood. The observed limits of normality are from 96 to 116 per cent for men and from 90 to 110 per cent for women; the possible limits calculated on a

6. Price-Jones, C.: J. Path. & Bact. **34**:779, 1931.

statistical basis are from 95.6 to 117.2 per cent for men and from 85 to 111.5 per cent for women (Price-Jones).[6] We have also taken Price-Jones'[6] normal values for the color index, namely, from 0.97 to 1.07 for men and from 0.91 to 1.08 for women.

Estimations of the average volume of red cells and hemoglobin saturation were made, a capillary hematocrit being used. For obvious reasons, this is the only method practicable for children, from whom it is undesirable and frequently impossible to obtain large quantities of blood. Although in the past such micromethods have been condemned as unreliable, with the use of accurately calibrated tubes and careful attention to detail they have proved in our experience exact methods of estimation. The method employed is one elaborated by the late Dr. R. J. Gittins, pathologist to the Children's Hospital, the details of which, with the results obtained in various cases of anemia, are shortly to be published. Briefly the method is as follows:

> Four or 5 drops of blood, obtained by pricking a finger, is run into a small tube containing a little heparin and a lead shot. When thorough mixing has occurred, the capillary hematocrit tube is filled and spun in the centrifuge at 8,000 revolutions per minute until all the cells are packed in the one end and no further packing occurs. The length of the column of packed red cells is then measured and compared with the length of the column of blood taken. The percentage of packed red cells in the specimen is thus determined, and from this value and the red cell count and percentage of hemoglobin, the average volume for the red cells and the hemoglobin saturation are calculated.

We have chosen to express the results as indexes rather than as the mean corpuscular volume and the mean concentration of corpuscular hemoglobin, because our method gives lower hematocrit values than the macromethod, as the result of closer packing of the red cells associated with the more rapid spinning, and therefore our values for the mean corpuscular volume and the mean concentration of corpuscular hemoglobin are not comparable with those obtained by workers who employed the macromethod.

Volume Index.—This index represents the ratio of the mean volume of a single red cell to the average normal volume, calculated by dividing the volume of packed red cells expressed in percentages of the normal volume by the number of cells expressed in percentage of the normal counts.

Saturation Index.—This value is the color index divided by the volume index, or, in other words, the ratio of the mean concentration of corpuscular hemoglobin to the normal concentration. The hemoglobin expressed in percentage of the normal value is divided by the number of packed cells expressed in percentage of the normal count. The limits of normality for both the volume and the saturation indexes may be taken as 0.9 and 1.1 (Haden[7]).

7. Haden, R. L.: Arch. Int. Med. **49**:1032 (June) 1932.

Diameters of red cells were measured, and their distribution curves were plotted, the technic of Price-Jones [8] being employed. This examination demonstrates minor variations from the normal value, such as a slight degree of anisocytosis, which signifies a disturbance in erythropoiesis and which may not be detected by other methods.

The diameters of 500 red cells were measured in microns and plotted on a graph (fig. 15). The average value for these cells is known as the mean diameter. A mean diameter greater than 7.718 or less than 6.686 microns is almost certainly abnormal; one which is

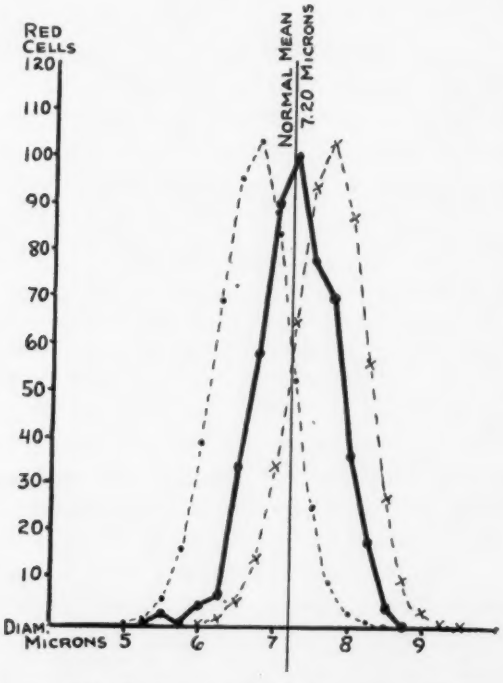

Fig. 15 (case 2).—Distribution curves of the mean cell diameters, expressed in microns, calculated by the method of Price-Jones. In this figure and in figures 16 and 17 the ideal curve for the smallest mean diameter within normal limits (-3σ, or 6.686 microns) is indicated by a line of dots and dashes; that for the largest mean diameter within normal limits ($+3\sigma$, or 7.718 microns), by a line of dashes and crosses, and the distribution curve for the mean red cell diameter (7.276 microns), by a solid line and dots. The standard deviation is equal to ± 0.502 microns, and the coefficient of variation, to 6.87 per cent.

greater than 7.546 or less than 6.854 microns is probably abnormal. Ideal curves for the largest (7.718 microns) and the smallest (6.686

8. Price-Jones, C.: Red Blood Cell Diameters, New York, Oxford University Press, 1933.

microns mean diameter within normal limits are included in the graph. By counting the cells the diameters of which fall outside these limits, the percentages of microcytes and macrocytes are determined. The width of the curve shows the degree of anisocytosis, and this is expressed mathematically as the percentage of variability (v); normally this value lies between 5.46 and 7.26 per cent; values higher than 7.26 per cent denote an abnormal degree of anisocytosis (Price-Jones [8]).

The patients in this series had never been examined hematologically during the early acute phase of the disorder, and we are unable to prove that the children showing a normal blood picture had ever been anemic. We feel safe, however, in assuming that in a large proportion of the cases reviewed (probably from 60 to 70 per cent) the patient was anemic at some period of the illness. In certain cases there was history of pallor; there was a greater incidence of anemia in the cases in which steatorrhea was still shown, and the literature on celiac disease contains many references to the frequency with which anemia occurs as a complication of the disorder. Thus, Thaysen [9] recorded hypochromic anemia in twenty-one of twenty-nine cases of active celiac disease. Herter [5] found hypochromic anemia in each of five patients whom he studied, and other observers have reported similar findings (Whipple,[10] Tileston and Underhill [11] and Fanconi [12]).

With the exception of the patient in case 2, who had been taking ½ drachm (1.84 cc.) of Marmite daily for many years, the subjects of this review had had no specific treatment for anemia when the first examinations of the blood were made, and any cure would therefore appear to have been spontaneous, the result of cessation of the celiac disease process.

Certain of the patients showing anemia were reexamined later, and we were able to observe others after the administration of iron. In other cases more than one examination of the blood was carried out when the first count showed certain peculiarities of the erythrocyte in the absence of anemia. The peculiarities will be mentioned later.

In table 21 are shown the results of the initial investigations and the records of subsequent confirmatory counts, the sex of the patient, the age in 1933 and a brief review of the clinical features in the case. The normal values for the various determinations are included, and all abnormal results are indicated in italics. The cases are arranged in order of the age of the patient.

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9. Thaysen, T. E. H.: Gee's Syndrome, the Coeliac Affection, Copenhagen, 1931.

10. Whipple G. H.: Bull. Johns Hopkins Hosp. **18**:382, 1907.

11. Tileston, W., and Underhill, F. B.: Am. J. M. Sc. **165**:625, 1923.

12. Fanconi, G.: Abhandl. a. d. Kinderh. (supp. Jahrb. f. Kinderh.) **21**:1, 1928.

TABLE 21.—*Summary of Results of Clinical and Laboratory Study in Eighteen Cases of Celiac Disease*

Case No.	Patient	Sex	Age in 1933, Yrs.	Date of Examination of Blood	No. of Red Cells, per Cu.Mm.	Hemoglobin, Percentage	Color Index	Volume Index	Saturation Index	Mean Diameter of Red Cells, Microns	Standard Deviation (σ), Microns	Percentage Variability (v)	Microcytosis or Macrocytosis, Percentage	Age at Onset of Disease, Yrs.	Age at Commencement of Treatment, Yrs.	Clinical Details
1	L. H.	F	23		No hematologic examination											
2	R. D.	M	18	10/24/33	5,010,000	102	1.00	1.01	0.99	7.276	0.500	6.87	None	3	10½	Severe condition neglected; treatment intermittent; no recent vitamin D therapy; advanced rickets
3	D. B.	F	18	10/31/33	4,750,000	94	0.99	0.93	1.06	7.027	0.463	6.59	None	2	7¾	Severe celiac disease; cured 3 yr.; full diet; normal bones
4	M. R.	F	18	7/20/33	5,130,000	95	0.92	....	....	7.281	0.510	7.01	None	..	..	Severe condition; cured 8 yr.; full diet; normal bones
				11/28/33	5,210,000	108	1.04	0.96	1.08	6.968	0.468	6.72	None	4	5	
5	M. G.	F	16	7/17/33	5,140,000	97	0.94	0.95	1.00	7.284	0.452	6.20	None	1¼	4	Moderately severe celiac disease; cured 7 yr.; normal bones
6	H. B.	F	15	11/28/33	5,700,000	106	0.93	0.92	1.01	7.141	0.496	6.94	None	4	6½	Moderately severe condition; cured 4 yr.; normal bones
7	S. P.	F	14		No hematologic examination											
8	L. M.	F	13	7/20/33	5,100,000	81	0.80	0.74	1.07	6.987	0.569	8.14	Microcytosis 1	2	3	Moderately severe condition; cured 6 yr.; full diet; normal bones

9	J. B.	F	13	9/ 7/33	4,400,000	57	0.65	0.75	0.86	6.716	0.637	9.49	Microcytosis 6	1½	7	Moderately severe condition; somewhat neglected for many years; cured 1 yr.; bones normal
10	A. R.	M	12	3/22/33	4.6	52	0.56	0.77	0.73	6.737	0.630	9.34	Microcytosis 4.4	2	5	Moderately severe condition, still active; treatment at home somewhat defective; normal bones; fat-restricted diet
11	G. P.	M	11½	8/14/33	5,600,000	82	0.73	0.70	1.05	7.221	0.624	8.68		2	5	Moderately severe condition, still active; fat-restricted diet; poor absorption of fats still; osteoporosis of bones
12	O. A.	F	11	10/19/32 9/ 7/33	4,750,000 4,000,000	90 89	0.95 1.11	.... 1.10	.... 1.01	..... 6.758	0.547	8.09	Microcytosis 0.6	1	2	Severe condition, still active; fat-restricted diet still maintained; normal bones
13	M. C.	F	10⅝	7/27/33	4,360,000	82	0.94	0.87	1.06	6.765	0.419	6.20		2	4	Severe condition; cured 4 yr.; full diet; normal bones
14	D. S.	F	10	9/14/33	4,800,000	95	1.00	0.99	1.00	6.331	0.513	8.06	Microcytosis 31.4	1	3½	Moderately severe condition; cured 2 yr.; full diet; normal bones
				2/12/33	4,650,000	96	1.03	1.02	1.01	6.772	0.489	7.25	0.4			
15	D.See	F	10	8/ 3/33	5,550,000	77	0.70	0.70	0.98	7.016	0.526	7.50		2	3	Mild condition, still active; fat-restricted diet still continued; normal bones
16	R. C.	M	9	11/27/33	4.82	94	0.98	0.94	1.03	7.300	0.520	7.01		2	3	Moderately severe condition; cured 4 yr.; full diet; normal bones
17	L. P.	F	8	9/ 7/33	4,960,000	93	0.95	0.93	1.01	7.216	0.548	7.60		1	2½	Moderately severe condition; cured 4 yr.; full diet; normal bones
18	E. L.	F	7	8/31/33	4,230,000	78	0.92	0.98	0.92	7.307	0.532	7.28	Macrocytosis 0.2	1	2	Moderately severe condition; still slight failure to absorb fats but full diet for 18 mo.; normal bones
				6/20/34	4,100,000	88	1.07	1.07	1.00	6.448	0.474	7.36	Microcytosis 22.4			

A glance at the table shows the higher proportion of cases of abnormality in the younger members of the series, and on dividing the patients into two groups, viz., those still showing steatorrhea and those recovered from the celiac disorder, it is found that of the six patients with signs of activity, four (60 per cent) showed anemia; in one instance (case 10) this was of moderate severity (hemoglobin 52 per cent), and in the other three (cases 11, 15 and 18), of mild degree only (hemoglobin 82, 77 and 78 per cent, respectively). Of the patients who did not recover, three (30 per cent) showed anemia, one (case 9) of moderate severity (hemoglobin 57 per cent) and the remaining two (cases 8 and 13) of mild degree (hemoglobin 81 and 82 per cent, respectively). In six of the seven cases of anemia it was of the typical hypochromic microcytic type. The red cell count was slightly reduced in one instance only (case 10). Values for hemoglobin varied from 52 to 82 per cent. The size of the red cells, as calculated from the hematocrit, was small in every case, the volume indexes varying from 0.56 to 0.8. The mean red cell diameters were normal in three cases, while in the three remaining cases the measurements were low and lay outside the values of 6.854 to 7.546 microns regarded by Price-Jones as the probable limits of normality. These results are interesting and illustrate the greater delicacy of the hematocrit determinations and estimations of cell volume as compared with results obtained by methods involving estimations of red cell diameter in the determination of the average size of the red cells. The saturation index was low in each of the two cases in which well marked degrees of anemia were shown—a finding that is usual in any case of anemia due to deficiency in iron, since the red cells are supplied with a poor quota of hemoglobin pigment. Definite microcytosis was found in three of the six cases, and in five abnormal degrees of anisocytosis were shown. In the cases in this series which we studied we did not observe [1] the macrocytosis described by Bennett, Hunter and Vaughan in their cases of hypochromic anemia associated with celiac disease. (The macrocytosis with a count of 0.2 per cent which was present in case 18 on Aug. 31, 1933, was associated with a normal mean cell diameter and was probably of no significance.)

One patient (case 18) when first examined in August 1933 showed a mild degree of anemia. The red cell count was 4,230,000, the hemoglobin content 78 per cent, the color index 0.92, the volume index 0.98 and the saturation index 0.92. A normal mean cell diameter and a slight increase in the degree of anisocytosis were noted. When reexamination was made in June 1934, the hemoglobin had risen to 88 per cent and the color index to 1.07, suggesting that at the first observation the patient was the subject of mild hypochromic anemia. This instance makes a total of seven cases of hypochromic anemia of greater or less

severity in a series of sixteen. The same patient at the second examination and on several subsequent examinations showed a peculiarity of the red cells characterized by a small diameter and a normal cell volume suggesting a cell of more globular type, such as is described in cases of acholuric jaundice. Further reference to this is made in the next paragraph. In case 17 slightly increased anisocytosis, as determined by the Price-Jones curve for red cell distribution, was shown, the only evidence of dyshematopoiesis and usually the last abnormality of the blood picture to disappear in the cure of hypochromic anemia.

In three of the cases studied (cases 12, 14 and 18) a peculiarity of the erythrocytes was presented, namely, a normal cell volume in association with a small mean cell diameter in the absence of anemia. The

TABLE 22.—*Summary of Results of Hematologic Study in Three Cases of Celiac Disease with Microcytosis*

Case No.	Date of Examination	Red Cells	Hemoglobin, Percentage	Color Index	Volume Index	Saturation Index	Mean Diameter of Red Cells, Microns	Standard Deviation, Microns	Percentage Variability	Microcytosis or Macrocytosis, Percentage
14	9/14/33	4,800,000	95	1.00	0.99	1.00	6.331	0.513	8.06	Microcytosis, 31.4
	12/12/33	4,650,000	96	1.03	1.02	1.01	6.722	0.489	7.25	Microcytosis, 0.4
12	9/ 7/33	4,000,000	89	1.11	1.10	1.01	6.758	0.547	8.09	Microcytosis, 0.6
	11/27/33	4,470,000	96	1.08	1.00	1.07	7.509	0.518	6.90	
	4/ 9/34	4,660,000	98	1.05	1.02	1.03	7.223	0.460	6.38	
18	8/31/33	4,230,000	78	0.92	0.98	0.92	7.307	0.532	7.28	Macrocytosis, 0.2
	6/20/34	4,100,000	88	1.07	1.07	1.00	6.448	0.474	7.36	Microcytosis, 22.4
	8/31/34									
	10:00 a.m.	.....	..	....	....	....	6.467	0.378	5.85	Microcytosis, 23.4
	4:00 p.m.	.....	..	....	....	....	6.523	0.409	6.27	19.4
	11:30 p.m. (after sleeping four hours)	.....	..	....	....	....	6.541	0.450	6.87	13.0

values for these cases are given in table 22. In case 14, the first examination in August 1933 showed a volume index of 0.99 and a mean red cell diameter of 6.331 microns, with the curve for red cell distribution shifted well to the left of the normal and indicating microcytosis with a count of 31.4 per cent (fig. 16 *A*). At a reexamination three months later, the volume index was 1.02, the mean cell diameter 6.772 microns and the degree of microcytosis 0.4 per cent (fig. 16 *B*); the distribution curve had moved to the right but still indicated microcytosis. In case 12, examination in September 1933 showed a similar abnormality, but on reexamination on two subsequent occasions the readings for the mean cell diameter were normal, and the volume indexes were not significantly altered (figs. 16 *C* and *D*). Case 18 has already been mentioned as an instance of mild hypochromic anemia. At the first examination, in August 1933, the volume index and the mean cell diameter were normal. In June 1934 reexamination of the patient did

not reveal anemia; the volume index had increased slightly (from 0.98 to 1.07), but the mean cell diameter was small (6.448 microns) and there was microcytosis with a count of 22.4 per cent (figs. 16 *E* and *F*). In August 1934 we had the opportunity of making blood films at intervals during a period of twenty-four hours, and in all of them the

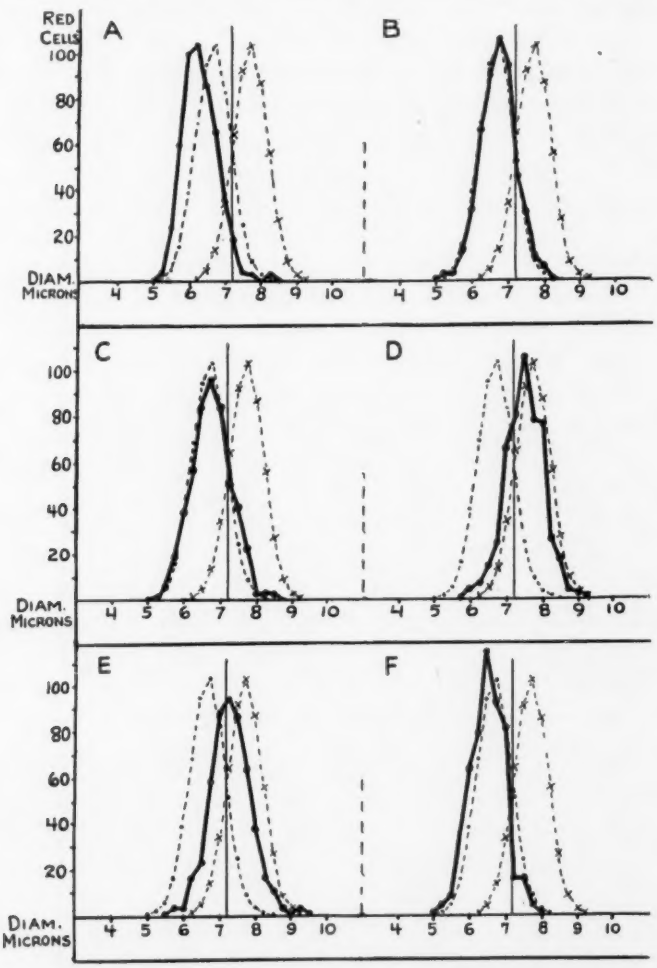


Fig. 16.—Price-Jones distribution curves for red cell diameter showing microcytosis in the absence of anemia. *A* shows the values in case 14 obtained in September 1933 and *B*, those obtained on Dec. 2, 1933. *C* shows the values in case 12 determined in Sept. 7, 1933, and *D*, those determined on Nov. 27, 1933. *E* shows the values in case 18 determined on Aug. 31, 1933, and *F*, those determined on June 20, 1934.

small mean cell diameter was evident in the Price-Jones curve. Films in all the cases showed small, deeply stained red cells, and it seems

probable that these cells were thicker and more spherical or globular than normal, a condition well recognized in acholuric jaundice but, as far as we know, not described in any other condition. There was no evidence of acholuric jaundice in these cases. The spleen was not clinically enlarged; no icterus was present at the time of the examination, and no history of icterus in the patient or the parents or other family history suggestive of icterus was obtained. The degree of fragility of the red corpuscles in saline solution was normal in every case, and there was no evidence of immaturity of the red cells in the stained films to suggest active regeneration of the marrow resulting from chronic hemolysis. The coefficient of variation (σ) was normal in each case, though when it was expressed as a percentage of the red cell diameter, i. e., percentage of variability (v), a value much higher than normal resulted because of the low mean cell diameter. In other words, the degree of anisocytosis of the red cells was normal, and the

TABLE 23.—*Comparison of Mean Red Cell Diameters Determined on Moist Preparations and Those Determined on Dried Stained Films*

Patient	Moist Preparations, Mean Cell Diameters, Microns		Dried Films, Fixed and Stained, Mean Cell Diameters, Microns
	Fresh Blood	Heparinized Blood	
A. W. J.	7.82	7.64	7.13
G. F. C.	7.64	7.78	6.8
E. F.	7.75	....	6.97
J. T. H.	7.70	....	7.03
C. W. S.	7.72	....	7.02

curve for red cell distribution retained its normal form and was shifted *en masse* to the left. It was thought that the findings might have resulted from excessive shrinkage during the process of drying of the blood film, but great care was always taken in making thin films and in insuring their rapid drying. We found no variability in the size of the cells in different parts of the films examined, and in two instances (cases 14 and 18) the same phenomenon was observed in subsequent examinations, when more than ordinary care was taken in making and staining the films. Ponder [13] criticized the methods of determination of the red cell diameter in which dried blood films such as those we used were employed. Recently we have compared the results of the measurements of red cell diameter on dried films stained by the method suggested by Price-Jones (1933) and those on wet preparations in which the cells remain in their own plasma or in heparinized plasma. Blood for the two or three preparations was taken from the same prick of the finger. The results are shown in table 23.

13. Ponder, E.: The Mammalian Red Cell and the Properties of Haemolytic Systems, Berlin, Verlagsbuchhandlung Gebrüder Borntraeger, 1934, vol. 6.

It will be observed that the reduction in red cell diameter due to drying, fixing and staining the cells is remarkably constant and varies from 8 to 11 per cent of the original mean cell diameter. These results are similar to those cited by Ponder.[13] Greater shrinkage than this has not been encountered, and we are satisfied that the small mean cell diameters described in these cases were not the result of technical error. In his book entitled "Red Blood Cell Diameters," Price-Jones [8] described the diurnal variations in the red cell diameter. The diameter of the red cell is found to be smallest on waking in the morning, and it is increased by violent exercise and diminished about 0.5 microns after forced breathing. All these changes occur without any significant alteration in the form of the distribution curve and were attributed by the author to alterations in the concentration of carbon dioxide in the blood, with consequent changes in the acid-base balance.

Wintrobe [14] and Haden [15] mentioned similar experiments in which the hematocrit was used and observations made on cell volume. They were unable to find any diurnal variation, and it seems probable, therefore, that the changes in cell diameter described by Price-Jones are associated with changes in the shape of the cell rather than with shrinkage and expansion. The results in the three cases of our series suggest that a similar process is at work, the result of changes in blood chemistry. In the cases in which the finding was inconstant, alterations in the mean cell diameter occurred without significant changes in cell volume. In case 18 the abnormality was present in each film taken during a period of twenty-four hours and showed no evidence of diurnal variation. The shift to the left appeared to be far greater than could be explained by alterations merely in the carbon dioxide tension of the blood. We have never observed this condition in any other disease except acholuric jaundice. All three children appeared to be in good health at the time of examination, and it seems probable that the changes described were the result of biochemical abnormality, a residual legacy of the celiac disorder, though we have had no opportunity of investigating such a possibility.

We were able to make subsequent observations on certain of the patients showing anemia at the time of the first examination and note the hematologic changes associated with recovery from the steatorrhea under a dietetic regimen and after the administration of medicinal iron. The details in such cases are given in table 24.

The patient in case 9 was observed in September 1933, when it was thought that she had been cured for one year. She was taking a full varied diet and showed a moderate degree of hypochromic microcytic

14. Wintrobe, M. M.: J. Lab. & Clin. Med. **17**:899, 1932.

15. Haden, R. L.: Am. J. M. Sc. **181**:597, 1931.

TABLE 24.—*Summary of Results of Hematologic Study and of Treatment in Four Cases of Celiac Disease with Anemia*

Case No.	Date of Examination	Red Cells, per Cu.Mm.	Hemoglobin, Percentage	Color Index	Volume Index	Saturation Index	Mean Diameter of Red Cells, Microns	Standard Deviation, Microns	Percentage Variability	Microcytosis, Percentage	Treatment
9	9/ 7/33	4,400,000	57	0.65	0.75	0.86	6.716	0.637	9.49	6.0	Full varied diet; reduced iron, 9 grains daily
	23/ 4/34	4,880,000	65	0.66	0.74	0.90	7.054	0.670	9.50	0.6	(April–July 1934)
	19/ 7/34	5,460,000	96	0.89	0.87	1.02	7.212	0.571	7.92	...	
18	31/ 8/33	4,230,000	78	0.92	0.98	0.92	7.307	0.532	7.28	...	Fat-restricted diet
	20/ 6/34	4,100,000	88	1.07	1.07	1.00	6.448	0.474	7.36	22.4	
8	20/ 7/33	5,100,000	81	0.80	0.74	1.07	6.982	0.569	8.14	1.0	Full, varied diet
	4/ 4/34	5,020,000	72	0.70	0.79	0.90	6.784	0.509	7.50	2.2	
11	14/ 8/33	5,600,000	82	0.73	0.70	1.05	7.221	0.624	8.68	...	Fat-restricted diet; reduced iron, 6 grains daily
	4/ 4/34	5,340,000	74	0.70	0.78	0.89	6.892	0.583	8.45	1.0	(April–July 1934)
	27/ 8/34	5,200,000	90	0.86	0.91	0.95	6.918	0.538	7.77	...	

anemia (table 24 and fig. 17 *A*). Seven months later, in April 1934, there was definite improvement in the blood picture: an increase of 7 per cent in the amount of hemoglobin, a normal mean cell diameter and a decrease in the degree of microcytosis. Anisocytosis, however, was even more marked, a usual occurrence in recovery from anemia (fig. 17 *B*). This spontaneous though slow improvement appeared to be the result of cessation of the celiac disorder and the consequent improved absorption of iron from the intestine. The child was then given massive doses of iron (reduced iron, 9 grains [583.2 mg.] daily) for three months. At the end of that time great hematologic improvement was shown, but the color index was still low, the red cell volume small and the degree of anisocytosis greater than normal (fig. 17 *C*). This case illustrates the peculiarity shown by many patients with celiac disease, namely, a difficulty in utilizing iron presented to them, both

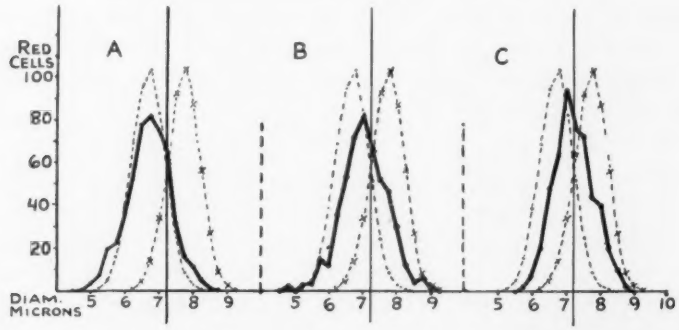


Fig. 17.—Price-Jones distribution curves for red cell diameter obtained in case 9, showing the process of cure of the microcytic anemia. *A* indicates the values determined on Sept. 7, 1933; *B*, those determined on April 23, 1934, and *C*, those determined on July 19, 1934.

during the active phase of the disease and after the cessation of steatorrhea. This partial or complete failure to absorb and utilize iron does not seem to depend on the presence or the severity of diarrhea; indeed, diarrhea was not a prominent feature in any case in the present series.

Case 18 again illustrates the slow recovery from anemia without the administration of medicinal iron.

The patient in case 8 when first examined in July 1933 had recovered from the celiac disorder and had been given a full varied diet for six years, but dyshematopoiesis of the hypochromic, microcytic type was still shown (table 24). Nine months later the anemia was even more severe. Roentgen examination of the bones showed no abnormality suggestive of an upset in the absorption of the calcium.

The patient in case 11 when first examined in August 1933 showed signs of poor absorption of fats, and mild hypochromic anemia. An increase in the degree of anemia was evident nine months later. Subsequent improvement occurred after three months of iron therapy.

The boy in case 10, aged 12, still had celiac disease of moderate severity after seven years of treatment. The slow response of the hypochromic anemia to treatment with iron and a slight relapse when the treatment was discontinued are shown in figure 18. The relapses noted

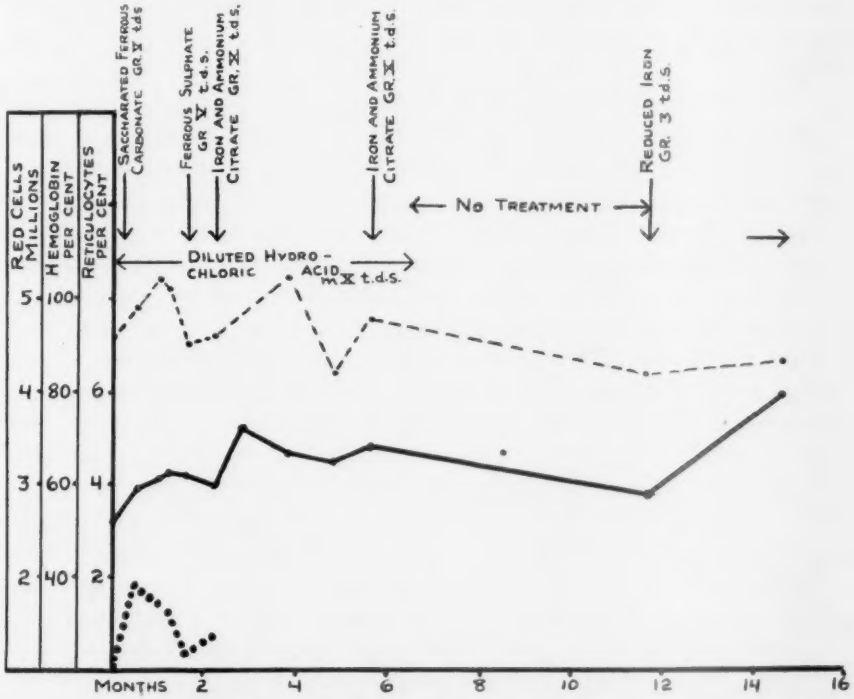


Fig. 18 (case 10).—Curves for red cells, hemoglobin and reticulocytes, showing the slow improvement in hypochromic anemia resulting from iron therapy and the relapse when such treatment was discontinued. In this chart, the curve for red cells is indicated by the line of dashes; that for the percentage of hemoglobin, by a solid line, and that for the percentage of reticulocytes, by the line of dots.

in these three cases did not appear to be due to an intestinal disturbance or intercurrent infection. Details in these cases are recorded in table 24.

One cannot but be impressed with the resemblance of the anemia in these cases to the idiopathic hypochromic microcytic anemia of middle age described by Witts [16] and others. The hematologic picture

16. Witts, L. J.: Guy's Hosp. Rep. **80**:253, 1930; Lancet **1**:549, 1932.

is identical; in both conditions there appears to be difficulty in absorbing or utilizing the relatively small amounts of iron present in the diet, and in the patients with celiac disease this does not appear to be necessarily associated with increased peristalsis of the intestines. In both conditions large doses of iron are required for cure, and relapses may occur when the treatment is discontinued.

Fractional analyses after a test meal were not carried out as part of the routine investigation in the cases in our series; only one patient (case 10) was examined in this way. He showed a moderate degree of anemia, but the acidity was normal. There was neither a history of soreness of the tongue nor evidence of glossitis on examination in any case.

We have endeavored to correlate the presence and degree of the disturbance of the blood with the other clinical features in the cases cited. With regard to the presence of steatorrhea, the following data were obtained: Of six patients who had not recovered from the celiac disorder, only four showed anemia, in one instance (case 10) of moderately severe degree, and two patients were hematologically normal. The condition of one of the last patients mentioned (case 2) was of striking interest. A youth aged 18, the victim of celiac disease of great severity and therapeutic neglect, on presenting himself in 1933 had gross deformities of the bones, osteoporosis, active rickets and persistent steatorrhea. In striking contrast to the upset in the fat metabolism, the blood picture was normal. Of the ten patients who recovered, only three were anemic—one to a moderately severe degree. In this instance (case 9) a full diet had been allowed for one year only, and subsequent examinations revealed the slow process of recovery from the anemia and cessation of intestinal disorder and steatorrhea (table 24 and fig. 17). Two patients showing lesser degrees of anemia had recovered and had taken full varied diets for four and six years, respectively, prior to the time of examination. It appears, therefore, that though absorption of iron tends to go hand in hand with that of fat and calcium and the anemia tends to disappear with improved absorption of fats, deficiency of iron may be evident many years after the cessation of steatorrhea and the stabilization of calcium metabolism. Conversely, normal absorption of iron may occur in the presence of steatorrhea and calcium starvation.

In the present series of sixteen cases there does not appear to have been a direct relationship between the presence or degree of anemia and any of the following factors:

1. The initial severity of the disorder.
2. The number of years during which the patient remained untreated.
3. The number of years since treatment was instituted.

4. In the cases of recovery, the number of years during which the patient was under dietetic treatment.

SUMMARY

In this paper are recorded observations, extending over many years, in eighteen cases of celiac disease in which the condition was diagnosed and treated during childhood together with an analysis of the immediate results of treatment in ninety-three cases of the acute form of the disorder.

It is seen that the condition develops during the early years of childhood, at any time after the age of 6 months. The greatest mortality rate is found in children about 2 years of age.

The eighteen cases include several instances of celiac disease in its most severe form, in which active rickets, osteoporosis and bony deformities were shown but in which the satisfactory results obtained by prolonged treatment and supervision of such patients during the early years of life were demonstrated.

The importance of long continued treatment with vitamin D or ultraviolet radiation in the cure of rickets, tetany and osteoporosis which were present in many of the cases is noted. Other vitamin deficiencies have not been observed in this series of cases.

The ability to absorb fat normally from the bowel and clinical and biochemical cure usually result after from two to six years of strict dietetic treatment, but clinical recovery may precede by one or two years the disappearance of all excess fat from the stool as determined by biochemical assay.

Improvement in nutrition and more rapid growth of bone accompany the control and subsequent cessation of the steatorrhea, and a particularly rapid increase in weight and height occurs at puberty, so that the end-result with regard to general nutrition, development and stature is particularly satisfactory. In the cases recorded in which adequate treatment had been maintained, little or no dwarfing was shown by the time adolescence was reached, and a normal ratio of height to weight was usually present. A notable reversion to a normal physical outline has been observed in the cases in which recovery took place, this being principally identified as diminution of the protuberance of the abdomen and increase in the gluteal outline to within normal proportions.

It has been specially interesting to observe during the favorable progress of the patients the eruption of good and anatomically normal teeth. In some cases in which adequate therapy was delayed the teeth were notably poor, and carious disease was evident.

Favorable progress has been associated with a more normal rate of growth of the hair and improvement in the texture of the skin. Sexual

development has not been inhibited, and even in the cases of more severe disease menstruation has commenced within the usual age period.

The effect of neglect of treatment is demonstrated in a case in a boy who at the age of 18 years still had steatorrhea, active rickets and gross deformities of the bones.

The blood picture has been studied in sixteen of the eighteen cases reviewed recently. Microcytic hypochromic anemia is commonly found in cases in which steatorrhea is still shown, and it may persist after cessation of the steatorrhea, even when a full varied diet is given.

The response to iron therapy may, in some cases, be slow, and relapses in the anemia may follow cessation of this treatment. The resemblance of this anemia to the idiopathic hypochromic anemia of adults is noted. In both conditions there appears to be difficulty in absorbing or utilizing relatively small quantities of iron. There is no apparent relationship between the presence or degree of anemia and the severity of the celiac process or the presence of other mineral or vitamin deficiencies. Cases are recorded in which somewhat globular red cells are shown, similar to those present in cases of familial hemolytic icterus, but in which there was no other evidence to support the diagnosis of this disease. The phenomenon is regarded as the result of an upset in the blood chemistry. In the case studied megalocytic or leuko-erythroblastic blood pictures were not present.

We are able to show that with increasing knowledge of the symptoms of the disorder more cases of celiac disease are being recognized by practitioners and the patients referred to the hospital for treatment during the period in which the disorder first becomes manifest, namely, the years of infancy and early childhood. The results of treatment at this stage are extremely gratifying. The essential steatorrhea disappears completely after a number of years of dietetic regimen, and the chronic invalidism, dwarfing, malnutrition, deformities and other complications found in the adult with celiac disease whose disease has escaped early recognition and treatment may be avoided.

Members of the staff of the Children's Hospital assisted in this study; Dr. Teall and Dr. Thorpe made the roentgenographic studies, and Miss Hickmans supplied the biochemical data.

The work was aided by a grant from the Medical Research Council.

Pediatrics in Art

RICKETS AND EXOPHTHALMOS

JOHN RUHRÄH, M.D.†
BALTIMORE

A painting by da Trevigo depicting rickets and exophthalmos.

Perhaps the commonest disease depicted in the paintings of the earlier artists is rickets, and there are few better examples than the Madonna and Child seen in the illustration. The painting is by Dario da Trevigo, a great friend and a pupil of Mantegna, and was painted in 1459. The enlargements of the ends of the long bones and the large square head are unmistakable. In addition, there is definite exophthalmos, the origin of which of course is doubtful, but the left eyeball is so much larger than the right that it suggests congenital glaucoma.

† Deceased.

Pediatric Biographies

CARL LEINER
1871-1930

A NOTE ON THE HISTORY OF ERYTHRODERMA DESQUAMATIVUM

JOHN RUHRÄH, M.D.†
BALTIMORE

Carl Leiner was born on Jan. 23, 1871, and was educated in Praha and Vienna. He was graduated in 1898 and began at once to devote his time to pediatrics, acting for a long time as assistant to Knöpfelmacher, but for the ten years preceding his death he was head physician to the Mautner-Markhof Children's Hospital in Vienna. He originated the intracutaneous method of vaccination against smallpox, and he was the first to observe postvaccinal encephalitis. While working in the Weichselbaum Institute he made observations on the virus of poliomyelitis and on other viruses and bacteria. He called attention to the annular erythema observed in cases of rheumatic endocarditis and did considerable work on diseases of the skin with which he was unusually familiar. He wrote the article on this subject for Jadassohn's "Handbuch der Haut-und Geschlechtskrankheiten." He was an unusual combination of clinician, practitioner, consultant and scientific investigator, both in clinical and in laboratory subjects. He was an interesting lecturer and taught both in German and in English. He died on April 24, 1930.

His name is associated with erythroderma desquamativum, or morbus Leiner, which he described in 1907. The following excerpt is from the article in the *British Journal of Children's Diseases*.[1]

ERYTHRODERMIA DESQUAMATIVA (UNIVERSAL DERMATITIS OF CHILDREN AT THE BREAST)

By Dr. Carl Leiner, Vienna

I WISH to draw attention to a peculiar disease of the skin, which spreads itself all over the body, but, which, however, must be distinguished from the specific forms of eruptions in infants, from the dermatitis exfoliativa Ritter, from the slight form of this disease of pemphigus contagiosus neonatorum, and also from the various other diseases of the skin, eczema, prurigo, etc.

† Deceased.

1. Leiner, C.: Brit. J. Child. Dis. **5**:244, 1908.

This dermatitis, about which I am reporting, presents a special type for itself, and it is of the greatest importance to be able to recognize it, for with few exceptions it only attacks children at the breast. This disease, far from being harmless, very often is extremely dangerous for the infants, and death from this form of dermatitis is not at all infrequent.

During the last five years I have made it my special task to study this form of dermatitis, and during this time I have closely observed forty-three cases of it in the Carolinen Children's Hospital in Vienna. Forty-one cases were in children nourished at the breast and two with the bottle. Twenty-eight were cured and fifteen died from the disease.

As a rule the children are brought for advice when the illness is already at its height, that is to say, at the end of the second or the beginning of the third month of life, seldom later. The children then present the picture of a universal dermatitis, which in all these specific cases bore the same aspect. The head presents the same appearance as in cases of seborrhoea. It is covered like a cap with thick yellow fatty scales and crusts, which may be easily removed from the

CARL LEINER
1871-1930

slightly inflamed, but in no wise ulcerated skin. The hair is sparse, on some spots matted. The eyebrows also present the same appearance as the scalp.

The rest of the face is almost entirely slightly inflamed and covered with thin yellow scales. Only the tip of the nose and the nostrils and the neighbouring parts of the cheek still bear a normal appearance, and it is only at the later stage that these parts are attacked by the eruption. The trunk is intensely red and at first covered with whitey-grey opaque scales, which later become lustrous. They may be easily removed from the slightly inflamed epidermis. The dorsal aspects of the extremities are more thickly covered with scales than the flexor. The hands and feet are red, but only in circumscribed spots. The nails also are affected by the disease and show various deformities, transverse and longitudinal grooves and small prominences and cavities of irregular form. The nail-bed is often hyperkeratotic, causing an abnormal convexity of the nails. In the folds of the skin and on the flexion side of the joints no scales are formed. Here the skin is of a dark red colour and oedematous. Only in the depths of the folds a covering of a dirty white colour is to be seen. Examination of the other organs proved them to be quite normal. The glands are only slightly swollen, about the size

of a cherry-stone; suppuration of the glands never occurs. The general health of the child is quite good, and the sleep is but little disturbed, this being due to the absence of itching. At this stage I could find no increase of temperature. On examination the urine proved quite normal. The mucous membrane of the mouth showed no remarkable changes. Changes are only to be found at this stage in the digestive organs and almost in every case, so that this seems to be one of the symptoms of this particular skin disease.

In the majority of the cases the further course was benign as the disease was cured in a few weeks. The hyperaemia of the skin, the intensity of the desquamation slowly ceases, the scales become thinner and smaller, and the skin gradually assumes a normal character. The pathological changes remain a long time in the folds of the scalp. Even when the skin disease takes a favourable course the general condition of the little patient's health is affected unfavourably by the illness. It loses weight, and this often very considerably. And this condition may last for some time, even for some months, till the child recovers and a regular and normal development is to be remarked.

I have already mentioned that the disease cannot always be cured; about one third of the patients die from it.

In spite of continuing the breast feeding the intestinal troubles come more and more to the front, the decrease in weight becomes more and more evident, so that the little sufferers are so terribly changed that they do not bear the slightest resemblance to the normal child at the breast.

The little one is emaciated and appears as if suffering from a severe illness. It is in a state of collapse, the face and extremities are of cyanotic colour, and the former is drawn with pain. The extremities become hypertonic; the whole skin is so dry that it often looks like parchment, and is covered with thin dry scales and traversed with fine rhagades. These rhagades are most severe round the mouth. On account of the infiltration of the lips and dryness of the skin the act of suckling often becomes very difficult or even impossible. Continual increasing cachexia and fever, associated with diarrhoea, soon cause death.

The post mortem examinations proved that, besides the pathological changes of the skin, there is always a severe degeneration of the muscle of the heart, fatty degeneration and infiltration of the liver, and catarrhal changes of the intestinal mucous membrane.

. . . This dermatitis is a real inflammation of the skin of the first few months of life, which has a peculiar interest, because it very rarely attacks other than suckling children, who often fall a sacrifice to this disease.

The aetiology is not yet quite clear. Probably the condition is an autotoxic erythema, which occurs in connection with the intestinal troubles. This dermatitis is to be carefully distinguished from the dermatitis exfoliativa of Ritter.

Obituaries

AUGUST CAILLÉ, M.D.
1854-1935

August Caillé died on Oct. 10, 1935, after a long and active life in the practice of medicine, a profession for which he was fitted by education and habit of mind.

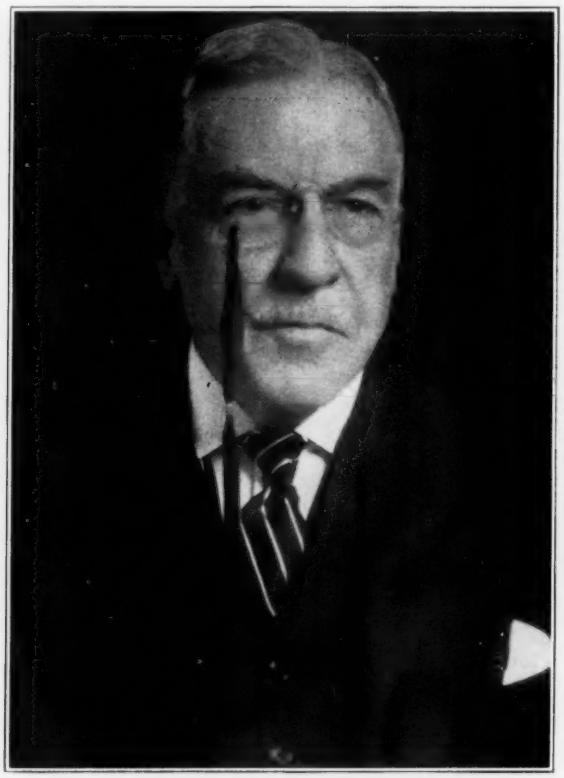
Dr. Caillé was born in Madison, Ind., on April 1, 1854, of French and German parentage, an ancestry that gave him facility in language and in literature. After his primary education he came to New York to study pharmacy and was graduated from the New York College of Pharmacy in 1873, but as he was desirous of becoming a physician he went abroad and entered the University of Würzburg, where he received his medical degree in 1877. At the university he was a good student and, strange as it may seem to his friends in America, an accomplished duelist. On his return to New York he matriculated at the College of Physicians and Surgeons of Columbia University and was given the degree of doctor of medicine in 1881. After this thorough scholastic medical training he engaged in general practice with a decided leaning toward pediatrics, in which specialty he was best known.

In 1888 he became connected with the New York Post-Graduate Medical School and Hospital in the department of pediatrics, and he continued the association to the end of his life, at which time he was emeritus professor and consulting physician. He was also visiting and consulting physician at the German Hospital, later renamed the Lenox Hill Hospital, and at the Convalescent Home for Babies, Sea Cliff, N. Y. He served the Isabella Home and Hospital as visiting physician and more recently as a consultant physician.

Dr. Caillé was progressive in his ideas and formulated them in his lectures and discussions. At a period when there was an aroused interest in infantile diarrhea and in its prevention by sterilization of milk for infant feeding, he advocated Soxhlet's apparatus for home use to lessen the dangers of intestinal infection. He demonstrated spinal puncture, stomach washing and O'Dwyer's method of intubation, and he also devised a number of instruments of a practical character.

He was a member of local and national medical societies and was recognized by his confrères in his election to the presidency of the American Pediatric Society in 1904, to the chairmanship of the Pediatric Section of the New York Academy of Medicine in 1891 and to office in other medical organizations.

As a man with good judgment in medical teaching and practice, with high standards of conduct in his profession, Dr. Caillé's opinion was sought by his medical associates for his knowledge of disease. He was said to be a link between the old and the new—the old because he was a keen student and observer in clinical medicine; the new, because he was ever ready to accept scientific aid that helped to explain and improve clinical methods.



AUGUST CAILLÉ, M.D.
1854-1935

He contributed to the medical literature in current publications and in the volumes "Differential Diagnosis and Treatment of Disease" in 1906 and "Prevention and Treatment of Disease" in 1918, which were well received by physicians and commended for the practical information they contained. Among Dr. Caillé's contributions to the meetings of the American Pediatric Society a few may be mentioned, viz.: "Lumbar Puncture," "Chart and Record for Clinical Diagnosis: Laryngeal Stenosis," "Sarcoma of the Suprarenal Capsule" and "Sudden

Death due to Enlarged Thymus Gland." Physicians who heard these papers were impressed with the author's ability to record symptoms clearly, and the reports were accepted as honest interpretations of his studies.

In 1908 Dr. Caillé was made a first lieutenant in the medical reserve corps of the United States Army, and in 1917 he received his commission as major.

The University of Würzburg gave him an agreeable surprise when in June 1927, the fiftieth anniversary of his graduation, it sent to him a new diploma, in lieu of his old one, with the congratulations of the medical faculty on his services in the healing art.

A practitioner, teacher and writer, Dr. Caillé had an esteemed position among the members of the medical profession. He left a record of a life of earnest endeavor and accomplishment.

W. L. C.

News and Comment

SOCIETY NEWS

Scientific Exhibit, Kansas City, Mo.—Application blanks for space in the scientific exhibit at the Kansas City session of the American Medical Association are now available. The Committee on Scientific Exhibit requires that all applicants fill out the regular form. Applications close Jan. 27, 1936. The representative of the Section on Pediatrics to the Scientific Exhibit is Dr. F. Thomas Mitchell, 376 South Bellevue Boulevard, Memphis, Tenn. Application blanks may be obtained from Dr. Mitchell or from the Director, Scientific Exhibit, 535 North Dearborn Street, Chicago.

New England Health Education Association.—The New England Health Education Association will hold the following meetings during 1936:

On January 14, at the Massachusetts Institute of Technology, Cambridge, there will be an address on "What Health Educators should not Teach about Communicable Diseases" by Dr. Gaylord Anderson of the Massachusetts State Department of Public Health.

The School Nurses' Section will have meetings in February, March, April and May on the first Tuesday of the month, covering various topics interesting to this section. The full-time Teachers' Section will meet February 18, March 17 and April 21, with a similar program, while the Class Room Teachers' Section will meet February 11, May 10 and April 14, with programs interesting to that group.

GENERAL

American Board of Pediatrics.—The next examination of the American Board of Pediatrics will be held just preceding the meeting of the American Medical Association at Kansas City, Mo., on Saturday, May 9.

The American Board of Pediatrics wishes to call the attention of all pediatricians to the fact that after September 1936 no applicant with ten years' experience or more will be certified without examination.

Physicians Certified by American Board of Pediatrics.—The following have been certified by the American Board of Pediatrics since the last report:

John Aikman, Rochester, N. Y.; Arthur Forrest Anderson, New York; Emily P. Bacon, Philadelphia; Edward Louis Bauer, Philadelphia; Arthur Wight Benson, Troy, N. Y.; Joseph Brennemann, Chicago; Kinsey Mansfield Buck, Memphis, Tenn.; Lloyd Blackwell Dickey, San Francisco; Emanuel Friedman, Denver; Joel J. Hobson, Memphis, Tenn.; Marvin Israel, Buffalo; Harry J. Jacobson, Memphis, Tenn.; John A. Johnson, Olean, N. Y.; Kenneth Thompson Knode, South Bend, Ind.; Frederic W. Lathrop, Plainfield, N. J.; Abraham M. Litvak, Brooklyn; Charles Fremont McKhann Jr., Boston; William Watson McKibben, Miami, Fla.; John A. Monfort, Brooklyn; Herbert L. Moon, Seattle; Grover Francis Powers, New Haven, Conn.; Joseph C. Regan, Brooklyn; C. Luverne Smith, Seattle; Caldwell B. Summers, Kansas City, Mo.; Frank Vander Bogert, Schenectady, N. Y.; Norman Carl Wetzel, Cleveland; Lawson Wilkins, Baltimore; Luvia M. Willard, Jamaica, N. Y.; James J. York, Schenectady, N. Y.; Jacob Rosenblum, Brooklyn; Maurice M. Malen, Philadelphia; Sydney Nussbaum, Brooklyn; Henry W. Straus, Brooklyn; Max Palinsky, Brooklyn; Frederick C. Hunt, New York; John E. Brown Jr., Columbus, Ohio; John Dorsey Craig, New York.

In this group eight candidates took the examination. At the examination, which was held in Philadelphia on Oct. 10, 1935, seventeen took the examination, and

nine failed. Of the eight who passed, one was in Group I, five in Group II and two in Group III. Of those who failed, four were in Group I and five in Group II. None of the failures was in Group III.

PERSONAL

Dr. Joseph I. Linde, Clinical Professor of Pediatrics, Yale University Medical School, has been appointed Health Officer for New Haven, Conn., the position formerly held by Dr. John L. Rice, now Health Commissioner of New York City.

DEATHS

Dr. José Garcia del Diestro, a Spanish pediatrician and one of the founders of *Archivos españoles de pediatría,* died recently in Madrid.

For many years he was director of the National School of Child Hygiene and was well known in his own country and abroad.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

THE EFFECT OF PARATHORMONE ON BASAL METABOLISM OF NORMAL DOGS. I. E. STECK, D. S. MILLER and C. I. REED, Am. J. Physiol. **110**:1 (Nov.) 1934.

Large doses of parathyroid extract administered to normal dogs do not increase the basal metabolism as was noted following the administration of viosterol. It is concluded that the parathyroids are not directly involved in the metabolic response of dogs to viosterol.

NOURSE, Cleveland.

STUDIES ON THE PHYSIOLOGY OF THE PARATHYROID GLANDS: VII. SOME RESPONSES OF NORMAL HUMAN KIDNEYS AND BLOOD TO INTRAVENOUS PARATHYROID EXTRACT. READ ELLSWORTH and JOHN EAGER HOWARD, Bull. Johns Hopkins Hosp. **55**:296 (Nov.) 1934.

The salient facts that the authors wished to ascertain were, first, whether the increased excretion of phosphorus in the urine, which was previously observed in patients with hypoparathyroidism, occurred regularly in normal persons and, second, if it did occur, whether there was an associated change in the calcium and inorganic phosphorus levels of the blood. Observations on the volume of the urine, the urine chlorides, the p_H of the urine and urea clearances were made.

The data presented here represent the results of single experiments on six "normal" persons and of three experiments on one patient with hypoparathyroidism. For the so-called normal persons patients were selected who were convalescent from an acute illness and who, while under observation for some time, had shown no evidence of renal or metabolic disease. The authors summarize the results as follows:

Following the intravenous injection of 40 units of parathyroid extract in normal persons there was an immediate outpouring of phosphorus in the urine. There was diuresis in some instances, but in others this did not occur. The urea clearance was not markedly altered; the excretion of chloride was diminished rather than augmented; the p_H of the urine tended to shift to a more alkaline range. There was a relatively slight fall in the plasma inorganic phosphorus. The serum calcium in several instances, instead of rising, tended to fall. The theoretical implications of these findings are briefly discussed.

LYTTLE, New York.

CONCERNING THE FUNCTION OF THE PINEAL BODY. W. SAPHIR, Endocrinology **18**:625 (Sept.-Oct.) 1934.

A relationship between the pineal gland and sexual development has been assumed, because patients with tumors of this gland have offered the most impressive pictures of precocious puberty or macrogenitosomia praecox. But contradictory findings are reported from experimental work.

Therefore it was thought worth while to implant human pineal bodies intramuscularly into thirty-six white mice. There was no inhibition of the sexual cycles of adult mice or gonadotrophic influence in infantile mice. But in castrated mice the material was found capable of producing estrus. This would suggest that the clinical picture of pubertas praecox in cases of pineal tumors would have to be explained on the basis of an increased secretion due to the active stimulating effect of the tumor.

JACOBSEN, Buffalo.

RADIOLOGIC STUDY OF THE ESOPHAGUS IN INFANCY. PAUL AIMÉ and MARCEL LELONG, J. de radiol. et d'électrol. **18**:466 (Sept.) 1934.

Observation of a hundred normal infants showed that the esophagus assumes several forms during the act of nursing, the most common being that of a large pocket so distended as to be equal in breadth or to exceed the shadow of the spinal column. Its contents vary. Sometimes its lumen is entirely filled by an accumulation of air, which often persists between feedings. Sometimes it is filled partly with air and partly by opaque liquid; in this type the air is in the form of two or three separate bubbles, and at each act of deglutition more air is swallowed than fluid. These and similar findings occur in the erect position. In the horizontal posture the size of the esophagus is less, and the contents are principally opaque. In normal deglutition the liquid contents are carried onward by energetic waves of esophageal peristalsis, their weight alone not being sufficient for propulsion. In the hypopharynx the contractive movement is brisk, less so farther down. Aerophagy is less pronounced when a semisolid is fed by spoon than with a fluid meal. The infantile cardia opposes but feeble resistance to reflux of gastric contents, but contraction of the esophageal walls is more forcible than in the adult.

VINTON, Brooklyn.

ACTION OF RADIATION ON CHOLESTEROL. E. and H. BIANCANI, Progrès méd., Nov. 28, 1934, p. 1859.

Increase in both the skin and the blood cholesterol has been shown to take place following exposure to sunlight, ultraviolet rays and infra-red rays. The authors suggest that this action is one of mobilization and excretion and is of value in subjects who show a tendency to the precipitation of cholesterol in various parts of the body.

LESLIE, Evanston, Ill.

THE VEGETABLE INSULINS. HENRI LABBÉ, Progrès méd., Nov. 28, 1934, p. 1867.

Substances acting like insulin in producing hypoglycemia and utilization of carbohydrates have been isolated from many vegetables. These are as yet imperfectly purified, but interesting results have already been obtained in cases of diabetes mellitus. With improvement of purification better and more consistent results may be expected.

LESLIE, Evanston, Ill.

IODINE OF THE THYROID. G. ANDREASSI and M. TALENTI, Arch. di farmacol. sper. **57**:169, 1934.

Examination of the thyroids from thirty persons in Rome showed an average of 0.0026 Gm. per gram of fresh thyroid substance. The average for men was 0.0025 and for women 0.0028.

KUGELMASS, New York.

FURTHER INVESTIGATIONS ON THE INFLUENCE OF THE ENDOCRINE SYSTEM ON CHOLESTEREMIA. E. INGLESSI, Clin. pediat. **16**:935 (Nov.) 1934.

Inglessi studied the effect of the administration of gland extracts to dogs, estimating the blood cholesterol over a period of about eight hours after injection in each instance. Extracts of thymus and parathyroid caused consistent reduction in the cholesterol value when this was determined at the end of two hours after injection. Extract of adrenal cortex, however, caused varying results in the different animals and in the same animal on different occasions.

DOOLEY, New York.

THE THYMUS OF HYPOPHYSECTOMIZED DOGS. B. A. HOUSSAY and J. M. LASCANO GONZÁLEZ, Rev. Soc. argent. de biol. **10**:241 (Aug.) 1934.

The data up to the present on the state of the thymus in hypophysectomized dogs are not in accord. Aschner described an abnormally increased persistence of

the thymus in hypophysectomized dogs that retained their infantile characteristics. Cushing, in 1912, found in hypophysectomized dogs and puppies a thymus rich in Hassall corpuscles and a lymphoid hyperplasia of the intestine. On the other hand, Ascoli and Legnani (1912) found an involution of the thymus in their hypophysectomized dogs. This was confirmed by Houssay and Hug in 1916, 1921 and 1923. In 1932, Kapran found total or almost total involution of the thymus in completely hypophysectomized puppies, but when only a partial hypophysectomy was done; the structure of the thymus was normal or not, according to how much hypophysis was left. Smith, in 1930, observed that hypophysectomy produced an immediate cessation of increase in the thymus in the rat, and that involution started. Neither involution nor histologic changes were constant, and he concluded that the hypophysis does not have a specific direct action on the thymus. The same variation of opinion has occurred in relation to adult human beings, but the majority of authors have found involution of the thymus in hypopituitarism and hypertrophy of the thymus in acromegaly.

The authors studied the thymus in sixteen hypophysectomized puppies. Involution of the thymus occurred in twelve and was absent in four. They concluded that involution of the thymus is frequent but not constant in hypophysectomized dogs. The cessation of growth of the thymus and its involution are phenomena produced by a common cause. It is probable that the involution of the thymus is due to the suppression of the growth hormone of the anterior lobe of the hypophysis.

HERRON, Spokane, Wash.

DEXTROSE TOLERANCE CURVES AND THE DEPENDENCE OF HYPERGLYCEMIA ON THE SPLEEN. E. S. LONDON and J. B. ENTIN, Ztschr. f. physiol. Chem. **225**:279, 1934.

London and Entin found, in studying dextrose tolerance curves, that the hyperglycemia was more marked and more sustained in dogs after the spleen had been removed.

HANSEN, Minneapolis.

INFLUENCE OF REDUCED IRON ON THE IMMUNITY OF RABBITS TO INFECTIONS. X. L. AMDEN, Sovet. pediat., no. 2, 1934, p. 30.

The fact that treatment with reduced iron increases the tonus of the whole organism suggested that it might increase the immunity to infection. Five experimental and five control rabbits were used. Each of the experimental rabbits received 0.1 Gm. of reduced iron for 1 kilogram of body weight during from eighteen to twenty-three days. After that time 0.5 cc. of streptococcus culture was introduced subcutaneously into the abdominal region. In eighteen hours four of the treated animals died, and the controls, though all sick, recovered.

Degeneration of parenchymatous organs and a slight amount of brown pigmentation were found in the reticulo-endothelial system of three rabbits. From this experiment Amden concluded that the introduction of iron into the body increases the sensitivity to infection. It was impossible to establish any great amount of change in the morphologic structure of the reticulo-endothelial system as a result of the iron treatment. The resistance of the animal to the micro-organisms had no direct relation to the quality of the red blood cells.

SEMENENKO-MCKHANN, Boston.

INFLUENCE OF PREGNANT URINE ON THE DEVELOPMENT OF GROWING RABBITS. Y. MATSUURA, J. Pediat. (Tokyo), Dec. 20, 1934, no. 415, p. 1711.

Matsuura injected subcutaneously 5 cc. of urine from women in the second trimester of pregnancy into young rabbits and noted marked hypertrophy of the uterus and mammary glands and a slight hypertrophy of the thyroid and testicles, but a distinct atrophy of the thymus. Other organs and the general growth of the animals showed no effect.

KATO, Chicago.

Nutrition

THE CLINICAL ASPECTS OF INFANT FEEDING. PHILIP S. POTTER, Arch. Pediat. **51**:310 (May) 1934.

This article adds little or nothing to the knowledge of this subject.

WADDELL JR., University, Va.

INTESTINAL INTOXICATION. ROY P. FORBES, Arch. Pediat. **51**:320 (May) 1934.

Forbes discusses the changes in the treatment of this type of disease over a period of years and the effect of such changes on the mortality from diarrheal diseases. In his small series of cases the mortality rate has fallen from nearly 100 per cent to less than 20 per cent within a period of fifteen years; the most significant drop occurred after the recent introduction of venoclysis. Due credit is accorded hospitalization in such cases, which makes possible greater facilities for the safe and frequent administration of water, salts and blood.

WADDELL JR., University, Va.

SYMPTOMS OF VIOSTEROL OVERDOSAGE IN HUMAN SUBJECTS. C. I. REED, J. A. M. A. **102**:1745 (May 26) 1934.

While much has been written and implied about the danger from excessive doses of viosterol because it is recognized as an extremely potent substance, this fact does not militate against its use as a therapeutic agent if proper precautions are observed. While it is probable that toxicity and hypercalcemia occur together frequently, it must be admitted that they are not interdependent but merely concurrent. Apprehension over the fact that excessive deposition of calcium in the soft tissues may occur even with relatively low dosages of viosterol does not seem justified. Toxicity in man may be recognized early by the appearance of frequency of urination and often persistent nausea and anorexia, followed by further evidence of gastro-intestinal irritability. The administration of highly concentrated viosterol to three hundred human subjects ranging from 7 to 72 years produced symptoms of toxicity in forty-three. The doses ranged from 3,000 to 2,760,000 international units daily, or a maximum of 920 times the normal antirachitic dose of 3,000 international units.

BONAR, Salt Lake City.

THE VITAMINS AND RESISTANCE TO INFECTION. ELIZABETH CHANT ROBERTSON, Medicine **13**:123 (May) 1934.

Robertson reviews the literature on the relation of the vitamins to infection and immunity and comes to the following conclusions:

1. *Vitamins A and D.*—There is no definite evidence to show that immune reactions of animals deficient in these vitamins are inferior to those of adequately fed controls. Clinical evidence, however, shows that marked deficiency of these vitamins is associated with numerous infections, and it is possible that mild degrees of infection may result in reduced resistance. The mass of evidence suggests that decreased resistance to infection occurs in animals suffering from a marked and prolonged deficiency of fat-soluble vitamins. Respiratory infections seem to be benefited by the addition of vitamins A and D to the diet. The onset of infection in persons whose diet is low in these vitamins increases their need for these factors, and it is probable that some of the tissues become partially depleted. It seems that the human lungs are particularly prone to be affected by deficiency of these vitamins.

2. *Vitamin A.*—There is a general as well as a local (epithelial) decrease in resistance in vitamin A-deficient animals, and resistance is reduced quite early in the deficiency, before signs of ill health appear. In disease beneficial effects follow the administration of vitamin A only when the patient has been on a diet deficient in this vitamin.

3. *Vitamin D.*—Antibody production probably is not reduced in rachitic animals, though the evidence is conflicting. Practically all the evidence seems to point toward an increased susceptibility to infection in animals with marked rickets (pigs, rats and infants). This deficiency may be associated with the seasonal incidence of respiratory infection in the northern climate. A great majority of investigators have shown that animals lacking in vitamin D are more susceptible to artificially induced infections. In tuberculosis small doses of vitamin D have been beneficial. Increased resistance following small doses of ultraviolet rays often occurs, but this may possibly be related to rays other than the antirachitic ones.

4. *Vitamin B (B_1 and B_2).*—The process of phagocytosis seems to be depressed in vitamin B complex deficiency, though reports are conflicting. A great variety of infections have been shown to be more frequently fatal or more easily induced in animals with marked vitamin B deficiency, but not in those with slight deficiency. The average diet contains small quantities of vitamin B_1. Yeast is apparently of value at times in acne and furunculosis, but results are conflicting as to its actual value in clinical infections.

5. *Vitamin C.*—While cutaneous reactivity is decreased in vitamin C deficiency, there is little evidence to show that the immune reactions of the blood are changed. Human beings with manifest or latent scurvy are more susceptible to infections than normal persons, and the infections are more severe in the former. Oral infections, especially pyorrhea, are said to result from a deficiency of vitamin C in the diet. Most workers have found that scorbutic guinea-pigs are more susceptible to infections, especially to tuberculosis, than normal guinea-pigs. Both clinically and experimentally, it has been found that infections tend to precipitate acute scurvy in vitamin C-deficient animals. Certain workers have found that the addition of vitamin C to the diet of tuberculous patients aids in the treatment of the disease.

McBryde, Durham, N. C.

Hypoglycemia and Ketosis: Their Relationship to Chronic Antral Disease and Bronchiectasis. C. Sippe, M. J. Australia **1**:675 (May 26) 1934.

Sippe offers evidence to support the theory that hypoglycemia and ketosis are factors in the etiology of chronic sinus infection and nontuberculous pulmonary fibrosis, and that these conditions are frequently associated with an exudative diathesis.

Cases of chronic sinusitis with acetonuria in which the condition was relieved by high dextrose, low fat diets are cited. Cases of hypoglycemia with asthmatic attacks, headaches and bronchiectasis (early) also are reported as those in which high dextrose diets were of benefit. In advanced cases of bronchiectasis and pulmonary fibrosis resulting from a long-standing sinus infection the condition was not benefited by dextrose therapy.

The explanation offered is that dextrose dehydrates the protein particles in the blood and at the same time causes retention of water in the tissues. It also causes a reduction in the precipitation of protein particles on the lining of the upper respiratory tract, which is responsible for the edema and congestion there.

Gonce, Madison, Wis.

Anorexia in Children. F. Cacciapuoti, Clin. pediat. **16**:291 (July) 1934.

The author gives an adequate review of the subject but presents no facts which may not be found in the standard literature on this condition.

Dooley, New York.

Modification of Serum Protein and of the Protein Quotient in Experimental Beriberi and Scurvy. D. Gorda, Clin. pediat. **16**:547 (July) 1934.

Experimental beriberi in pigeons causes a reduction in the total protein, this reduction being due to a decrease in the serum albumin. The albumin-globulin

ratio approaches unity, or even reverses. In experimental scurvy in guinea-pigs the results are similar, but there is usually an increase in the serum globulin.

DOOLEY, New York.

METHOD OF DETERMINATION OF THE BODY SURFACE AND ITS IMPORTANCE IN CALCULATING THE FOOD REQUIREMENTS OF THE NURSING INFANT. C. BARTALINI, Riv. di clin. pediat. **32**:654 (June) 1934.

This article is in reply to criticisms raised by Trambusti to the author's acceptance of an indirect method of determining the body surface. The direct method is open to practical difficulties, which overbalance a possibly greater accuracy. The author prefers the method of DuBois.

HIGGINS, Boston.

HYDROLABILITY IN EARLY INFANCY. SALVADOR E. BURGHI, Arch. de pediat. d. Uruguay **5**:225 (June) 1934.

Acquired hydrolability occurs more often than the congenital form. It is usually observed in the dystrophic infant and is generally caused by superimposed infections. It is more often observed in hospitalized infants; more than 90 per cent of these show some degree of atrophy. It is rare in an urban clientele, because these infants are better nourished. After certain infections, such as prolonged digestive disturbances, quantitative or qualitative hypo-alimentation and certain intoxications with acidosis, the histologic structure and the functional capacity of the cells are altered with respect to retention of water. A normal hydrostable constitution can be transformed to a hydrolabile one.

SCHLUTZ, Chicago.

INFANTILE ATHREPSIA TREATED WITH THYROID EXTRACT AND ASSOCIATED WITH A HYPERGENITAL SYNDROME OF A PARADOXICAL NATURE. I. SIMIAN, Spitalul **54**:171 (April) 1934.

A patient with athrepsia of the type of Parrot was saved from his grave state by opotherapy that was administered when the child was thought past relief, owing to the lack of success of the usual other measures of treatment.

The child on entering the dispensary weighed 6,650 Gm. and remained at that weight for an entire month. Dietetic treatment, vitamin treatment and the administration of calcium by mouth or injections brought no improvement. To the surprise of the physicians opotherapy with the administration of thyroid gland lowered the weight for the first few days, but soon thereafter there was a slow, steady increase during the entire period of treatment. The general state of the child has improved from the point of view of weight, height and disposition.

The child presented a definite endocrine disturbance at the end of the treatment. The penis measured 5½ cm. at 4 years and 8 months; there was unilateral cryptorchidism, which became bilateral on lying down. The endocrine disturbance accompanied by precocious macrogenitosomia is considered paradoxic because cryptorchidism never accompanies macrogenitosomia. In fact, this syndrome is associated not only with the presence of the testicles but a definite increase in their size.

AUTHOR'S SUMMARY.

ACTION OF DIFFERENT KINDS OF LIGHT ON GLYCOLYSIS. E. KEESER, Arch. f. exper. Path. u. Pharmakol. **170**:500, 1933.

Irradiation of a 0.1 per cent solution of glucose (buffered by phosphate) with red light for thirty minutes in the presence of yeast cells accelerated the decrease in the reducing power; white, green or blue light has little effect. Similar results were obtained with fructose, as well as in the glycolysis of glucose or fructose by guinea-pig serum. Irradiation (five hours) of ox serum with visible light did not alter its reducing power or its content of inorganic phosphorus; ultraviolet irradiation increased the reducing power but did not change the inorganic phos-

phorus content. Rabbits irradiated with visible light exhibited a reduction in the number of white blood corpuscles, but apart from a temporary eosinophilia no change in the differential count occurred.

KUGELMASS, New York.

PHYSICOCHEMICAL STUDIES OF THE INFANT'S STOOL. THEOPHIL BAUMANN, Monatschr. f. Kinderh. **60**:81, 1934.

In a long and interesting article Baumann has attempted to solve two questions. The first half is devoted to a study of the factors influencing the hydrogen ion concentration of the stool, the second half to a study of the buffer of the stool.

As regards the hydrogen ion concentration of the stool, he studied the concentration of calcium and phosphate, the calcium-phosphate quotient, the total alkali, volatile fatty acids, heavy volatile and nonvolatile fatty acids, water content, bacteria and the reaction of the food itself. He can attribute the reaction of the stool to no individual factor, but to the combination of all these factors, which in general is the relation of the fermenting substances to the buffer. The stool of the breast-fed infant shows a low p_H, a low concentration of calcium and phosphate, a high calcium-phosphorus quotient and a considerable quantity of organic acid. The stools of infants on cow's milk and mixed feeding have a high calcium and phosphate concentration but a low calcium-phosphate quotient, low quantities of organic acids and a p_H close to neutral. Feeding apples and bananas results in either acid or alkaline stools, depending on other factors of the diet; a low concentration of calcium and phosphorus, and a relatively high calcium-phosphate quotient.

In studying the buffer Baumann followed the same procedures. He concludes that in cow's milk feeding the buffer is largely due to the absolute quantity of calcium and phosphate. As these may exist in combinations, such as tertiary, secondary and even primary phosphate, it is possible that several buffer systems may be at work. Organic acids are also concerned in their combinations with salts. In the stool of infants on breast milk, apple and banana feedings the buffer is due mainly to the organic acids. The p_H of the stool stands in no relation to the buffer, nor does the calcium-phosphorus quotient or the water content. Baumann concludes that there are probably other active buffers which he has not isolated.

GERSTLEY, Chicago.

ANOREXIA IN CHILDHOOD AND ITS TREATMENT. A. BRATUSCH-MARRAIN, Wien. klin. Wchnschr. **46**:1032 (Aug. 18) 1933.

Disturbances of appetite, according to Bratusch-Marrain, are among the most frequent disorders with which the pediatrician has to deal. There are two chief forms: (*a*) acute and subacute anorexia in connection (as symptoms) with various illnesses and (*b*) chronic anorexia, not conditioned organically but caused by errors in training. In infancy the child best regulates its nourishment according to its own desires. The approximate necessary amount of food can be figured out; then the amount must be individualized according to appetite.

Chronic anorexia occurs in three forms: 1. The child is robust but "has no appetite." It is usually found that the child eats enough but not as much as the parents think is necessary. Treatment by enlightenment of the parents is more difficult than one would believe. 2. The child looks well (or sometimes does not) but does not eat at meal-time. Questioning usually brings out that the child eats between meals. Treatment consists in getting the child to eat regularly, if the parents will cooperate; otherwise, a hunger diet and medicine may be effective. 3. The child eats poorly. Often there is a really poor nutritional state. Questioning may reveal that the child is merely being contrary. He is coaxed and rewarded, the question of food being overemphasized. Often the child seeks consciously or unconsciously to become the center of attention. Threats and punishment become even worse than coaxing, because the child is in a state of fear before meals. Enlightening the parents as to the reasons for the anorexia is usually of no avail. A hunger diet and medicine may sometimes be effective, or a diagnosis of

"disease of the stomach" may be made. The prophylaxis consists in letting the natural appetite have free play. An important maxim to follow is that the child may eat but must not be forced to eat. It is difficult for mothers to attain this point of view. The parents must learn that the healthy child is by no means always the fat one, and that thinness at certain ages is to be looked on as normal.

ABT, Chicago.

ORIGIN, METABOLISM AND ELIMINATION OF CHOLESTEROL IN THE ANIMAL ORGANISM. S. MINOVICI, M. VANGHELOVICI and G. MARZA, Bull. Soc. chim. Romania **15**:137, 1933.

Dogs placed on a diet of boiled potatoes lost weight and showed a rapid loss in blood cholesterol. The addition of egg-white caused a sharp rise in the cholesterol level the first two days, but the level returned to normal. Oleic acid added to the diet caused a marked increase in cholesterol formation. Casein and egg-yolk both caused a marked increase also, but it is known that egg-yolk contains cholesterol. In order to demonstrate that this increase was due to oleic acid, the total cholesterol content was determined. For this purpose two species of insects, the yellow Blatta germanica and the black Stylopyga orientalis, were used. Losses in cholesterol were observed if the diet contained either dextrose, starch, casein and starch or margaric acid and starch. Stearic acid and starch caused no loss or gain. If the diet contained oleic acid there was a marked increase in cholesterol. Black field-mice and white laboratory rats gave analogous results. Starved rats fed oleic acid showed a marked increase in cholesterol, while stearic acid produced no change. Following the injection of oleic acid into the blood stream below the liver there was a greater amount of cholesterol in the blood leaving the liver than there was in the portal vein. Hence the liver is capable of synthesizing cholesterol from oleic acid, and this can be converted to cholic acid.

KUGELMASS, New York.

THE PART PLAYED BY THE LIVER IN THE WATER METABOLISM (A HYDROPHILIA TEST). B. A. POLEEV, Vrach. delo **17**:251, 1934.

The author determined the rate of resorption of a blister in patients with a swollen liver, as well as in controls (patients with a normal liver). He found the lapse of time necessary for this to be normally seventy-five minutes on the average; this corresponds to the data of Hygenheimer (sixty minutes) and of McClure (more than an hour). Swelling of the liver, no matter what the cause may have been (even in patients with heart disease suffering from decompensation but not from edema of the foregoing state), leads to an acceleration of the hydrophilic reaction.

The part played by the liver in the water metabolism being above doubt, the latter results may be explained by assuming that in the author's case the last-named function of the liver was not impaired at all or so slightly that it did not show in the hydrophilic reaction.

YAMPOLSKY, Atlanta, Ga.

EXPERIMENTAL HYPERGLYCEMIA. KUNIZO FUKUDA and YUKIHARU TAKAYANAGI, Nagoya J. M. Sc. **7**:43, 1933.

The intravenous injection of peptone caused no change in the dextrose content of the blood of dogs which had fasted for from two to five days, but well nourished dogs showed hyperglycemia. It is concluded that the deposits of sugar in the liver are present in two forms, the more susceptible being mobilized by peptone. Epinephrine is able to mobilize the less susceptible portion as well, whereas peptone is not. Thyroid extracts and thyroxine produce hyperglycemia followed by hypoglycemia from opposite actions, first on mobilization from the liver and secondarily from increased utilization by the tissues.

KUGELMASS, New York.

Composition of Growth: III. Infantile Atrophy. Bengt Hamilton and Nathan W. Shock, Acta pædiat. **15**:314 (June 5) 1934.

This is a balance study of the electrolyte metabolism in a marantic male infant 2 months old. The authors summarize their results as follows:

"In a case of chronic malnutrition (infantile atrophy), metabolism experiments were conducted over a period of 106 days, 60 of which the infant actually spent on the metabolism bed. In 5 periods, covering 41 days, there was a gain in weight. The retentions of sodium, potassium, chloride, calcium, magnesium and nitrogen were calculated per kilogram gain in weight from these 5 periods, and compared with normal figures previously obtained by Swanson.

"It was found that in respect to the retentions of sodium and potassium, the atrophic infant differed markedly from the normal infants. The sodium retention was low, probably indicating that the new tissues formed were not holding a normal amount of interstitial fluids. The potassium retention was very high, both absolutely and in relation to the retention of nitrogen. It is argued that this increased retention of potassium indicates either the repair of intracellular dehydration, or the formation of cells abnormally rich in fluids."

McCune, New York.

An Experimental Investigation Concerning the Resistance of Vitamin C in Milk to Pasteurization in Vacuo. G. Rundberg, Acta pædiat. **15**:357 (June 5) 1934.

Despite the large amount of work which has been devoted to the problem, the question of the antiscorbutic potency of raw cow's milk still remains unanswered. Many investigators contend that raw cow's milk contains little or no vitamin C, whereas others have found it efficient in preventing scurvy in guinea-pigs. The controversy has brought to light one point which is probably important, namely, that the concentration of vitamin C is somewhat dependent on the diet of the milk-producing animal. Milk obtained in summer has greater protective powers than that yielded in winter.

Since opinions vary so much concerning the vitamin C content of raw milk, it is not surprising to find even greater uncertainty with regard to the antiscorbutic effect of pasteurized milk. It is well known that vitamin C is readily oxidized. When it is heated in the presence of air it rapidly loses its activity. However, it may be subjected to heat in an atmosphere free from oxygen without appreciable deterioration. Attempts to apply the information in a practical way to preserving the antiscorbutic properties of cow's milk have led to encouraging results in some quarters but have been entirely disappointing in others.

Rundberg reports the details and results of very carefully controlled experiments with guinea-pigs bearing both on the original vitamin C content of cow's milk and on the resistance of the substance to pasteurization in vacuo. The milk was obtained from one cow kept in pasture between June 19 and August 31. It was used within a few hours after milking.

In addition to suitable controls, there were four experimental groups: animals fed (1) raw milk, (2) raw milk from which the dissolved air had been evacuated, (3) raw milk pasteurized by heating one-half hour at 63 C. and (4) milk pasteurized in vacuo for the same time and at the same temperature. The size of the feedings varied from 5 to 10 cc. daily. The animals weighed between 300 and 400 Gm. at the beginning of the experiment.

Although the appearance of scurvy was delayed in the four groups of experimental animals when compared with the controls, it was not prevented in a single case. All the animals died of the disease. There was no significant difference in the effect of the various types of milk used.

Rundberg concludes that raw milk is relatively poor in vitamin C. Naturally it was not possible to draw any conclusions regarding the effect of pasteurization in vacuo since the untreated or raw milk could not be shown to have significant protective powers.

McCune, New York.

Acute Infections

WHOOPING COUGH AND ITS ROENTGENOLOGIC MANIFESTATIONS. FRANCESCO TECILAZIC, Pediatria **42**:921 (Aug. 1) 1934.

The author reports studies and observations on a series of patients with whooping cough, with particular emphasis on roentgenologic study. He is convinced that roentgenograms in whooping cough reproduce faithfully the anatomic alterations in the thorax. As early as the first ten days of the disease they demonstrated the characteristic annular formation of Pincherle, simple hilitis and the basal triangle of Gottche.

SIGNORELLI, New Orleans.

BACTERICIDAL POWER OF WHOLE BLOOD TOWARD THE DIPHTHERIA BACILLUS. P. SCHIAPARELLI and D. CAVALLERO, Riv. di clin. pediat. **32**:803 (July) 1934.

Guinea-pigs given subcutaneous injections of diphtheria bacilli show a bacteremia four or five hours after the injection; the bacteremia lasts about one hour. If the injection is intraperitoneal, the bacteremia appears in one hour and lasts one hour. With rabbits, intravenous injection results in a bacteremia lasting from two to two and one-half hours. Diphtheria bacilli are found in the organs only during the phase of the bacteremia.

The addition of an anticoagulant to the blood of the rabbit or guinea-pig in vitro inhibits completely the bactericidal power of the blood against diphtheria; this action is probably due to the destruction of complement. Intravenous injection of the anticoagulant increases the phase and the intensity of bacteremia. The quantity of diphtheria organisms tolerated by a normal rabbit is lethal to a rabbit treated with the anticoagulant.

The authors conclude that the bactericidal power of whole blood is an element of fundamental importance in preventing the diffusion of bacteria by the blood in the course of diphtheria.

HIGGINS, Boston.

TYPHOID BACTEREMIA IN CHILDREN: METHOD OF CULTURING. F. AUXILIA, Riv. di clin. pediat. **32**:818 (July) 1934.

The addition of a new anticoagulant, sodium polyanetolsulphonate, to blood diminishes the normal bactericidal power of blood probably by the destruction of complement. Its addition to blood withdrawn for blood culture from children with typhoid fever increased the incidence of positive cultures from 36.5 to 43.9 per cent.

HIGGINS, Boston.

PROPHYLAXIS AGAINST PERTUSSIS BY VACCINE. A. VENUTI, Riv. di clin. pediat. **32**:986 (Aug.) 1934.

In a children's institution, sixteen children from 2 to 4 years of age were in close direct contact with two patients with pertussis in the catarrhal stage; each of the sixteen received pertussis vaccine as a prophylactic measure, but pertussis developed in four. Among twenty-three infants indirectly exposed to these children and given pertussis vaccine pertussis developed in none.

HIGGINS, Boston.

PROPOSAL TO ESTABLISH A LAW MAKING IMMUNIZATION AGAINST DIPHTHERIA OBLIGATORY. RAUL CIBILS AGUIRRE, Arch. argent. de pediat. **5**:449 (Aug.) 1934.

In view of the fact that for more than ten years immunization against diphtheria has been practiced successfully and without harmful effect in many countries, including his own, the author recommends the establishment of a law making such immunization compulsory.

SCHLUTZ, Chicago.

ANTIDIPHTHERITIC IMMUNIZATION WITH ANATOXIN. V. ZERBINO, Arch. de pediat. d. Uruguay **6**:269 (July) 1934.

Immunization with diphtheria anatoxin is universally practiced and is an important factor in the prophylaxis against diphtheria. To have assurance of

maximum effectiveness a uniform technic must be followed. Zerbino recommends three injections given at weekly intervals. A certain percentage of the patients, especially those living in urban communities, may lose immunity within the first year, some in the second or third year. It is wise to control the cases in which immunization has been produced within the year. The author recommends a fourth injection of 2 cc. of the anatoxin regardless of the outcome of the Schick test.

One should always be on guard for persons who easily lose their immunity: children in the age range of from 1 to 4 years, subjects who live in exposed communities or where there is diphtheria in the family or where the parents have positive Schick reactions or children who are successfully immunized but lose their immunity within a year or a year and a half after vaccination.

In an epidemic of diphtheria Zerbino recommends a renewed immunization with 2 cc. of anatoxin to all immunized children, regardless of whether the Schick reaction was positive or negative.

SCHLUTZ, Chicago.

PURPURIC MEASLES. JULIO COMBY, Bol. Soc. cubana de pediat. **6**:93 (May) 1934.

Comby describes a case of this rare condition of which he has observed only five others. The disorder appears late in the stage of eruption and at the beginning of convalescence. It must be differentiated from the hemorrhagic form of measles. The eruption is purpuric and is confined entirely to the skin. There are no nasal hemorrhages and no bleeding from the throat, bowels, lung or urinary tract. The patients seem to be comparatively well, in contrast to the great prostration and fatal symptoms of the malignant hemorrhagic form. In the purpuric form of measles the initial eruption is transformed to a hemorrhagic area confined entirely to the skin and persisting during convalescence from the disease. There are no abnormal changes in the blood. No special therapy is indicated.

SCHLUTZ, Chicago.

INFLUENCE OF TONSILLAR ENUCLEATION ON SUBSEQUENT SCARLET FEVER AND DIPHTHERIA. A. VON ZSINDELY, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **138**: 195 (Aug. 22) 1934.

Von Zsindely made a comparative study of several thousand cases of scarlet fever and diphtheria which occurred before and after tonsillectomy. He found that in most cases tonsillectomy decreases the incidence of infection from both diseases. This decreased incidence after tonsillectomy seems, however, to decline parallel with the time which has elapsed after operation.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

VARICELLA AND SENSITIZATION BY LIGHT. A. S. VON MALLINCKRODT-HAUPT, Dermat. Wchnschr. **99**:917 (July 14) 1934.

Observations by the author tend to show that exposure to sunlight or to artificial ultraviolet radiation increases the number and changes the character of the varicella lesions which develop in the irradiated area.

TAUSSIG, San Francisco [ARCH. DERMAT & SYPH.]

PROPHYLACTIC AND THERAPEUTIC VALUE OF PERTUSSIS VACCINE. K. KUNDRATITZ, Med. Klin. **30**:1060 (Aug. 10) 1934.

Forty-eight children were given a course of pertussis vaccine, seven prophylactically, the rest therapeutically, with excellent results. The vaccine used was prepared by the Vienna Serotherapeutic Institute and was given in five injections (3, 4, 6, 8 and 8 billion organisms) at one or two day intervals. The cases were chiefly from private practice, and the disease occurred during three distinctly different epidemics.

DOOLEY, New York.

IMMUNE SERUM AND PATIENT'S SPINAL FLUID IN THE TREATMENT OF ACUTE POLIOMYELITIS. TÖRÖK, Med. Klin. **30**:1093 (Aug. 17) 1934.

Török treated forty-nine patients with acute poliomyelitis in the following manner: Equal parts of adult blood and of convalescent blood were injected intramuscularly in quantities varying from 30 to 50 cc. At the same time the patient's own spinal fluid was injected intramuscularly in quantities of from 15 to 20 cc., and this injection was repeated daily for several days. In comparing his results with those of Kramár and Liszka (*Orvosi hetil.* **77**:1081, 1933) in an analogous group of cases, Török finds that the double treatment appears to have a decided advantage. It would seem that the protean nature of this makes it inadvisable to draw conclusions from the results in such a small series of cases.

DOOLEY, New York.

THE PERIOD OF REST IN BED IN DIPHTHERIA. P. VON KISS, Monatschr. f. Kinderh. **60**:426, 1934.

Patients with diphtheria must stay in bed as long as there are any local signs of the disease. Further, they must remain there as long as any remote effects of the diphtheria toxin are manifest. If an electrocardiograph is available the patient should not get up until clinical symptoms disappear and the electrogram is normal in two leads. In the absence of an electrocardiograph the patient must be confined to bed for at least six weeks from the first symptoms.

GERSTLEY, Chicago.

EARLY SYMPTOMS OF THE INFECTIOUS DISEASES OF CHILDHOOD. F. VON BORMANN, München. med. Wchnschr. **81**:1236 (Aug. 10) 1934.

Bormann describes the insidious onset of diphtheria with slight fever, malaise and sometimes headache or abdominal pain but without symptoms referable to the throat. For this reason he emphasizes the importance of examining the throat of all sick children. Whenever diphtheria is even suspected clinically, the patient should receive antitoxin immediately, and no time should be lost in waiting for the report of cultures sent to a laboratory.

In contrast to diphtheria, scarlet fever has a sudden onset, with vomiting, headache, fever and pain on swallowing. The child is acutely ill and has a fiery red throat and a thick coating on the tongue.

The exanthem of measles is usually preceded by catarrhal symptoms and the presence of Koplik spots. Occasionally there is a confusing prodromal eruption simulating that of scarlet fever, but it lasts only a few hours.

The author also discusses pertussis, mumps, dysentery, the meningitides and poliomyelitis, without presenting anything of special interest.

BRAHDY, Mount Vernon, N. Y.

THE SCHICK AND DICK REACTIONS AND THE NASOPHARYNGEAL BACTERIAL FLORA OF NJENZEN ON THE KOLGUJEW ISLAND. W. N. ASBELEW and A. A. MARGO, Zentralbl. f. Bakt. (Abt. 1) **126**:212, 1932.

The authors tested 103 persons of different ages on the Kolgujew Island (69 degrees north latitude) for Schick and Dick reactions. Diphtheria and scarlet fever are not known to occur among these people. The Schick test was negative in all but one, an 8 year old girl. Similarly, the Dick test was negative in all but one instance and there it was doubtful. Skin anergy was excluded, as a group of Njenzen living on the mainland (33 persons tested) showed positive Schick tests in 12 per cent of cases and positive Dick reactions in 30 per cent. Tests for the presence of diphtheria antitoxin by Römer's method were not made.

No diphtheria carriers were found among 168 residents of the island who were examined. Streptococci were found in 84 per cent of the instances, hemolytic types in 3 cases.

CANNON, Chicago. [ARCH. PATH.]

THE CULTIVATION OF VACCINE VIRUS IN VITRO. F. BREINL, Zentralbl. f. Bakt. (Abt. 1) **127**:308, 1933.

A strain of vaccine virus was cultivated in Maitland's medium through a long series of passages. Less active multiplication was obtained when rabbit kidney, guinea-pig testis or guinea-pig kidney was used. Rabbit spleen or urine, plant tissues and yeast cells were useless. The growth-promoting substance was destroyed by heating at 45 C. for thirty minutes. The virus grew best in a range of p_H of from 6 to 9.2. It did not grow when deprived of oxygen.

CANNON, Chicago. [ARCH. PATH.]

THE SEROLOGY OF PERTUSSIS. M. GUNDEL and W. SCHLUETER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **81**:218, 1934.

According to Gundel and Schlueter, differentiation of the influenza and of the Bordet-Gengou bacilli is always possible. In addition to cultural differences, the bacilli of Bordet and Gengou produce local necrosis when a suspension of the live bacilli is injected intracutaneously; the influenza bacilli do not possess that property. However, the most important means of differentiation is the complement-fixation test. The antigen was prepared from a vaccine which is sold by one of the commercial houses in Germany. It contains 8,000,000,000 micro-organisms per cubic centimeter and is made from 48 hour old cultures killed in the water bath at 60 C. and preserved with 0.5 per cent phenol. The vaccine was centrifugated, suspended in 50 per cent alcohol, shaken for one hour and kept at 37 C. for twenty-four hours. Lecithin was added, and it was found that the optimum amount was 0.2 cc. for 1 cc. of the antigen. Such antigen proved highly specific and sensitive. A prolonged cultivation of Bordet-Gengou bacilli led occasionally to changes of their antigenic qualities. Strains were observed which gave doubtful results with the usual technic. They could be eliminated when the complement fixation was carried out at 0 C., at which temperature only true Bordet-Gengou bacilli reacted. Differentiation was also possible by means of adsorption of specific serums. Complement-fixation tests were positive with serums of patients suffering from pertussis in a large percentage of cases, and they were uniformly negative with serums from a large number of controls suffering from a variety of diseases. For reasons already mentioned, it is necessary to carry out two tests: one at 37 C., the other at 0 C. Of seventy serums from suspected patients, fifty-four gave positive results, three doubtful results, and thirteen negative results. The test was rarely positive during the first two weeks, particularly in infants less than 6 months of age. In artificially immunized children the complement-fixing antibodies appeared sooner and rose more rapidly than in patients suffering from spontaneous infections. According to Gundel and Schlueter, the lack of success of previous authors with the complement-fixation test in pertussis was due primarily to the frequent selection of improper strains of bacteria for the antigens.

DAVIDSOHN, Chicago. [ARCH. PATH.]

THE BLOOD ANTIGENS OF THE SHIGA DYSENTERY BACILLUS. F. SCHIFF, Ztschr. f. Immunitätsforsch. u. exper. Therap. **82**:46, 1934.

The Shiga dysentery bacilli are known to contain, in addition to the heterophilic (Forssman) antigen, two antigenic substances in common with human red corpuscles. One of them is the species-specific human blood antigen; the other is a group-specific antigen related to or identical with the human A_2 factor (Landsteiner) and with the 0 factor (Schiff). Schiff employed an immune serum which was produced in a goat by injections of Shiga dysentery bacilli. The serum agglutinated only weakly all human red corpuscles, but those of group 0 and of subgroup A_2 were agglutinated selectively in high dilutions. There are natural variants of Shiga dysentery bacilli which lack the heterophilic and the human blood antigens. Similar results can be obtained artificially by adding bacteriophage to the culture medium on which the Shiga bacilli are grown. The bacteriophage

deprives them of the heterophilic as well as of the human antigens. In view of the fact that ordinary culture medium contains peptone, which is antigenically related to the human blood group factor A, Schiff investigated the possibility that the Shiga bacilli get their human blood antigenic substances from their food. He grew them on a synthetic medium free from constituents of animal origin. The antigenic properties of the bacilli remained unchanged, proving that their origin is not dependent on the constitution of the culture medium.

DAVIDSOHN, Chicago. [ARCH. PATH.]

COMPLEMENT FIXATION IN HERPES ZOSTER AND CHICKENPOX. OLUF THOMSEN, Ztschr. f. Immunitätsforsch. u. exper. Therap. **82**:88, 1934.

The antigen was prepared from crusts of herpes zoster and from chickenpox lesions. The results of complement-fixation tests with the serums of eighty-eight patients with herpes zoster and fourteen patients with chickenpox were entirely negative. Thomsen calls attention to the recent report of Brain of England who obtained positive results with an antigen prepared from the vesicular fluid and negative results when crusts were used as antigen. Brain's work confirms some previously expressed opinions of a close serologic relationship between the two diseases.

DAVIDSOHN, Chicago. [ARCH. PATH.]

OPTIC NEURITIS AFTER IMMUNIZATION AGAINST RABIES. HASABE, Acta soc. ophth. jap. **38**:102 (July) 1934.

Hasabe draws attention to the unpleasant side effects of immunization against rabies consisting in paraplegia of the legs with paralysis of the bladder and rectum and occasionally ascending paralysis. Cases in which the eyes also are involved are unusual. He has recently observed a case of bilateral optic neuritis following immunization against rabies. A boy 10 years of age was bitten by a mad dog in August 1933. The modified Pasteur injection treatment was given, and fever, paresis of the legs, hyperesthesia of the skin, headache and general prostration followed. Seven days after the completion of the treatment the patient suddenly complained that vision in the right eye was affected. On examination, optic neuritis was found in both eyes. The pupil of the right eye was immobile. Repeated lumbar punctures had a most favorable influence on the ocular symptoms.

KNAPP, New York. [ARCH. OPHTH.]

SCARLET FEVER AND DIPHTHERIA IN TONSILLECTOMIZED CHILDREN. ULF NORDWALL, Acta pædiat. **15**:338 (June 5) 1934.

The published figures of Bradford, Doull, Kaiser and others suggest that persons whose tonsils have been removed exhibit a slightly diminished susceptibility to scarlet fever. There is no unanimity of opinion concerning the effect of tonsillectomy on the severity and duration of the disease and on the incidence of complications. Nordwall analyzed the records of 2,825 patients admitted to the wards for the patients with scarlet fever of the Stockholm Hospital for Infectious Diseases over a period of six years. About 5 per cent of these patients had had their tonsils removed. It was shown by accepted statistical methods that tonsillectomy did not influence the severity of the original illness, as judged by the degree of angina and the intensity of the eruption. With the exception of sinusitis, complications occurred just as often among those patients whose tonsils had been removed as among the others. Hemolytic streptococci persisted longer in the throats of those whose tonsils were still present; this fact did not prolong the duration of infectiousness as estimated by the number of secondary cases originating in persons exposed to these patients when they returned home.

There is some statistical evidence to support the contention that removal of tonsils increases resistance to diphtheria. However, Kaiser was unable to show a difference between the incidence of diphtheria in 2,200 children whose tonsils

were out and its occurrence among a like number who had not been operated on. In reviewing the records of 1,781 patients with diphtheria admitted to the Stockholm Hospital during a period of six years, Nordwall found it impracticable to draw a definite conclusion bearing on this point; he offers the impression that extirpation of tonsils does not significantly alter susceptibility to diphtheria. It was apparent from the statistical analysis of this case material that removal of the tonsils exercises a determining influence on the site of the formation of membrane in diphtheria. Pharyngeal localization is much more common when the tonsils are intact than when they have been removed. With the tonsils out it is more usual to find the membrane in the nose. Diphtherial infection assumes a malignant character more often in persons who retain their tonsils than in those who have had them out. Patients without tonsils suffer fewer complications.

McCUNE, New York.

A SEROLOGIC REACTION IN MALARIA (REACTION OF HENRY). C. M. DHONT JR., Nederl. tijdschr. v. geneesk. **78**:2188 (May 19) 1934.

The technic and principles of the test of Henry are described in detail; it is a new precipitation test of the serum of patients with malaria, founded principally on the fact that the pigment formed by the malarial parasites in the organism acts as an endo-antigen and in this way stimulates the formation of antisubstances. A review of the results obtained by different authors with this method is given. Dhont comes to the conclusion that a positive reaction of Henry points with great probability to the existence of a malarial infection, whereas a negative one excludes malaria.

VAN CREVELD, Amsterdam, The Netherlands.

TWO ATTACKS OF POLIOMYELITIS AT AN INTERVAL OF TWENTY-FOUR YEARS. M. TESDAL, Norsk mag. f. lægevidensk. **95**:978, 1934.

The literature contains reports of at least twelve instances of a second attack of poliomyelitis. In Tesdal's instance the first attack occurred at the age of 16 years, when both legs became paralyzed, and the second at the age of 40 years, when both arms became paralyzed.

EDITOR'S ABSTRACT. [ARCH. PATH.]

Chronic Infections

FREQUENCY OF TUBERCULOSIS IN EUROPE AND BRAZIL. GEORGE GUIMARES, Arch. de pediat., Rio de Janeiro **6**:819 (June) 1934.

Tuberculosis is much less frequent in Brazil than in Europe. Guimares believes that this is due to three factors: more sunshine, fewer large cities and a less rigorous climate.

SANFORD, Chicago.

DIAGNOSIS OF TUBERCULOSIS WITH PARTICULAR REFERENCE TO SKIN TESTS. GILBERTO G. ROMEIRO, Arch. de pediat., Rio de Janeiro **6**:931 (Aug.) 1934.

In a group of children who had had some contact with tuberculosis at the clinic in Rio de Janeiro 44.96 per cent gave positive reactions to the Pirquet test. Of these, twenty-six were boys and thirty-two girls. There were twenty-two children in the first year, fifteen in the second, four in the third, six in the fourth and one in each year thereafter up to 6 years.

SANFORD, Chicago.

A PREVENTORIUM FOR TUBERCULOSIS. ANTONIO G. DA SILVA, Arch. de pediat., Rio de Janeiro **6**:945 (Aug.) 1934.

Da Silva gives an interesting description of the Preventorium D. Amelia, which is situated on the Island of Paquetá in the Bay of Guanabara, Brazil. There are numerous photographs of the patients and buildings. Antonio Frasca has contributed a short article contained therein on the necessity of keeping the teeth of tuberculous children in good condition.

SANFORD, Chicago.

CASEOUS BRONCHOPNEUMONIA WITH CAVITY FORMATION. HECTOR MOURIGAN, Arch. de pediat. d. Uruguay **6**:322 (Aug.) 1934.

A mother with active tuberculosis had the care of her infant and nursed him for twenty-six days. After admission to the hospital he was fed diluted cow's milk. There was steady decline in weight, and shortly before death cough and dyspnea developed. There were comparatively few physical findings in the chest. The liver and spleen were enlarged. At autopsy caseous bronchopneumonia and a small cavity were noted. Generalized miliary tuberculosis was present in both lungs. The author is of the opinion that this condition was congenital in origin and not acquired postnatally.

SCHLUTZ, Chicago.

ANTITUBERCULOSIS PROPHYLAXIS, USING CALMETTE'S METHOD. ARLINDO DE ASSIS, J. de pediat., Rio de Janeiro **1**:340 (Sept.) 1934.

De Assis discusses the various arguments for and against Calmette's vaccine for tuberculosis. He has used it in the Liga Brasileira Contra Tuberculose on 20,000 infants and is certain that it answers every claim that has been made for it. He believes that it should be generally used in combating this condition.

SANFORD, Chicago.

CONGENITAL SYPHILIS. WALDEMAR RIBEIRO, J. de pediat., Rio de Janeiro **1**:364 (Sept.) 1934.

To combat congenital syphilis it is necessary to educate the public to the dangers of syphilis, diagnose syphilis in the pregnant woman and treat the mother during pregnancy. The child born of a syphilitic mother should have the benefit of all modern treatment for a period of not less than two years, even if symptoms are not apparent.

SANFORD, Chicago.

SYPHILITIC MENINGITIS IN A CHILD OF THREE MONTHS. FERNANDO M. GOMES, Mov. pediat. Belo Horizonte **1**:119 (Aug.) 1934.

The first symptoms were convulsions. The child recovered after treatment with twelve injections of arsphenamine, with supplementary treatment with mercurials and bismuth. He appeared entirely normal at the age of 6 months.

SANFORD, Chicago.

ANTITUBERCULOSIS VACCINATION WITH BCG. CLODOVEU DE OLIVERIA, Mov. pediat. Belo Horizonte **1**:123 (Aug.) 1934.

The author gives an excellent review of the cases of all the patients who have died as a result of vaccination with BCG. The total that he has found from a study of the literature is seventy-three.

SANFORD, Chicago.

VACCINATION WITH BCG IN A CHILDREN'S HOSPITAL. FRANCISCO DE SOUSA LIMA, Mov. pediat. Belo Horizonte **1**:135 (Aug.) 1934.

The author recommends vaccination during the first ten days of life. This is done by the oral administration of three doses of 0.02 Gm. of BCG at intervals of one day.

SANFORD, Chicago.

BLOOD CALCIUM AND CHOLESTEROL IN INFANTS WITH TUBERCULOSIS OF THE BONES. ANGELES and LUIS PÉREZ DEL RIO, Paidoterapia **13**:331 (Aug.) 1934.

Investigation of the blood calcium and cholesterol in fifty-nine cases of infants with tuberculosis of the bones revealed not a single case in which the calcium was below normal, but the cholesterol was diminished. On treatment the cholesterol value increases. Therefore the authors believe that frequent determinations of the cholesterol might be of value in determining the progress of the curative treatment.

HERRON, Spokane, Wash.

OPEN TUBERCULOSIS IN CHILDHOOD. G. WEBER and F. STÜRMLINGER, München. med. Wchnschr. **81**:976 (June 29) 1934.

The finding of tubercle bacilli in the contents of the stomach following gastric lavage carried out on tuberculous children in whom both clinical and roentgenologic examinations did not reveal open tuberculosis brought up the question of the infectiousness of such children. Most authors isolate such children when they are in the hospital, but some consider the danger of infecting other patients slight.

Weber and Stürmlinger exposed six guinea-pigs for three months in a ward of tuberculous children. Some of the children had pulmonary tuberculosis; others had tuberculosis of the glands, bones, joints or skin. The guinea-pigs were in cages kept on the floor or window sills of the ward. The children could take the animals out of the cages to play with or feed. The animals were removed during visiting hours to prevent infection from outside sources. During the test period several of the children had pertussis with the usual severe and prolonged coughing. Six control guinea-pigs were kept in a kitchen adjacent to the ward but were not exposed to any of the children.

After being in the ward three months the guinea-pigs were kept in a room for animals an additional three months. Tuberculin skin tests were then done, and all of them were negative. Autopsy failed to reveal tuberculosis grossly or microscopically. The results may be due to the small number of bacilli expectorated by these children and the hygienic surroundings in the ward. Strict isolation of all tuberculous children does not seem necessary.

BRAHDY, Mount Vernon, N. Y.

MORTALITY FROM TUBERCULOSIS. F. WILDTGRUBE, Ztschr. f. Gesundhführ. **1**:326, 1934.

Wildtgrube attempts to prove that statistics concerning the mortality from tuberculosis in infants show, over long periods of time, three different phases. The first phase shows a decrease of the total mortality from tuberculosis with an accompanying decrease of mortality from local as well as disseminated forms of tuberculosis. This he calls the phase of definite increase in immunologic conditions. The second phase leads to an increase in the mortality from disseminated forms and a slight increase in the total mortality. The mortality from localized forms either decreases or remains the same. This he regards as an expression of the impairment of immunologic conditions. The third phase is one in which the total mortality from tuberculosis decreases and the mortality from disseminated forms decreases, but the mortality from localized forms increases. This, he states, is a transitional phase. He believes that he has demonstrated these phases for larger cities, but not for smaller cities where the accumulation of data is too small for use.

REICHLE, Cleveland.

FUNCTIONAL ABILITY OF THE STOMACH IN PULMONARY TUBERCULOSIS. J. J. MOSHKOWSKY, Vrach. delo **16**:755, 1933.

The author conducted a series of gastric analyses on one hundred and twenty-four patients with pulmonary tuberculosis. His conclusions were as follows:

1. Most of the tuberculous patients show disturbances of the secretory function of the stomach.

2. The acidity of the gastric juice, the intensity of the tuberculous process and the degree of intoxication are correlated. Patients with compensated and mild forms of the disease generally show hyperacidity, while patients with decompensated forms are inclined toward gastric subacidity.

3. No strict parallelism was found between the intensity of the tuberculous process and the disturbances of the gastric secretion. Also, the changes in the chemistry of the gastric juice do not seem to be related to the complaints of the tuberculous patient.

4. In most cases the secretion reaches its maximum during the second hour after a test meal. Nevertheless, there is no reason to consider a delayed secretion as characteristic of the tuberculous patient.

5. Neither the method of double stimulants (according to Zimnitzky) nor Katsch's fraction method allow one to establish definite types of gastric secretion characteristic for tuberculosis.

6. In 88 per cent of the total number of cases the fasting stomach was found to contain gastric juice. Tuberculosis has a depressing influence on the functional activity of the stomach.

7. Though a severe tuberculous process is more frequently associated with a gastric subacidity, lack of constancy is the most characteristic feature of the gastric secretion in tuberculosis. Accordingly, subacidity of the gastric juice gives place to normal juice or to hyperacidity, as is found on repeated examinations.

8. The frequent heterochylia in tuberculosis would tend to prove that the depression of the secretory function is not caused by an organic insufficiency of the secretory apparatus but rather by a certain lack of the stability of the vegetative system.

9. The alkaline reserve of the blood was not found to be dependent on the acidity of the gastric juice.

BODER, Chicago.

THE SO-CALLED PARTICULAR FILTRABLE FORM OF TUBERCLE BACILLI. P. C. FLU, Nederl. tijdschr. v. geneesk. **78**:3019 (June 30) 1934.

The author proved that filtrates of tuberculous material passed through Chamberland L2 and L3 filters were free from the test microbes mixed with the material to be filtered and never caused signs of classic tuberculosis or of so-called ultra-tuberculosis. The criticism of these experiments by van Deinse is discussed, and his objections are disproved.

VAN CREVELD, Amsterdam, The Netherlands.

Internal Diseases

INTRAVENOUS GALACTOSE LIVER FUNCTION TEST. I. R. JANKELSON and H. H. LERNER, Am. J. Digest. Dis. **1**:310 (July) 1934.

This article describes an improvement of the old galactose liver function test of Bauer. Twenty-five grams of galactose is injected intravenously and blood specimens collected at thirty minute intervals for two hours. Normally the galactose disappears from the venous blood in one hour, the liver utilizing it. This phenomenon is purely of scientific importance and may prove later to be of practical importance because of its tests for liver function.

Seven subjects with normal livers and eight patients with pathologic conditions of the liver are reported on. There is a definite decrease in the rate of utilization of galactose in the patients who have a pathologic condition of the liver as compared with normal subjects. Minimal degrees of hepatic damage are not disclosed by this test, as the rate of utilization of the galactose may be normal.

The methods of procedure are given in the original article.

MORRISON, Savannah, Ga.

GAUCHER'S DISEASE: REPORT OF A CASE WITH PRESENTATION OF A TABLE DIFFERENTIATING THE LIPOID DISTURBANCES. AARON CAPPER, HERMAN EPSTEIN and ROBERT A. SCHLESS, Am. J. M. Sc. **188**:84 (July) 1934.

This disease is now regarded as a congenital, primary and familial constitutional disease in which lipoid kerasin is stored in large foam cells, the Gaucher cells. Gaucher's disease is especially prevalent in the Jewish race and is more common in females. A case in a 10 year old Jewish girl is reported. The Gaucher cells invade the spleen, liver, lymph nodes and bone marrow and may invade the thymus, tonsils, lymph tissue of the intestines and lungs and even the cerebral cortex in infancy. Hypochromic anemia and leukopenia developed although the latter is not

essential for diagnosis. The patient's disorders include a variety of symptoms related to the osseous system. A comprehensive comparative table of the various diseases due to disturbances in the lipoid metabolism is presented. The treatment is splenectomy (which is fatal in 20 per cent of the cases) or irradiation. Both are palliative measures only, although in the case reported marked improvement was noted.

HENSKE, Omaha.

ON THE INHERITANCE OF DIABETES MELLITUS: II. FURTHER ANALYSIS OF FAMILY HISTORIES. GREGORY PINCUS and PRISCILLA WHITE, Am. J. M. Sc. **188**:159 (Aug.) 1934.

Among the parents and siblings of a group of diabetic patients the reported incidence of diabetes is 300 cases in a total of 4,434 (6.7 per cent), whereas only 16 cases of diabetes were reported in a total of 1,296 parents and siblings of a group of nondiabetic patients (1.23 per cent). The difference between the percentages observed is statistically significant. When the assumption is made that diabetes develops in persons homozygous for a recessive gene (i. e., in genetically diabetic persons), it can be demonstrated that the ratio of diabetic to nondiabetic persons among the siblings of the diabetic patients conforms with the consequent expectations, provided that one assumes that potentially diabetic patients are subject to the ordinary chances of death before the disease develops. Employing differing data for the incidence causes little variation in the mendelian expectations. This is taken to indicate that so long as diabetes occurs in the fairly regular manner indicated by ordinary tables showing the incidence and so long as the chances of death indicated by the ordinary tables showing the expectancy of life apply, mendelian expectations will be satisfied. It is, therefore, highly probable that the development of diabetes mellitus depends primarily on the transmission of a single recessive gene. But the ordinary age-incidence relations indicate the operation of one or more secondary factors. The data at hand give no accurate clue as to the nature of these secondary factors.

HENSKE, Omaha.

TUMORS AND TUMOR-LIKE CONDITIONS OF THE LYMPHOCYTE, THE MYELOCYTE, THE ERYTHROCYTE AND THE RETICULUM CELL. G. R. CALLENDER, Am. J. Path. **10**:443 (July) 1934.

Callender has studied three hundred and eighty cases of disease of the lymph nodes and bone marrow which were submitted to the Lymphatic Tumor Division of the American Registry of Pathology between 1925 and 1934. The stem cells in this group are divided into lymphocytes, polymorphonuclear leukocytes, red blood corpuscles and monocytes or reticulo-endothelial cells (it is noted that there may be some objection to the latter two terms as synonyms). The classification of each stem cell tumor is then made. For the lymphocyte it is as follows: (1) reactions —lymphoma, lymphocytosis; (2) proliferations of the neoplastic type—acute and chronic leukemic lymphocytoma and diffuse and nodular aleukemic lymphocytoma; (3) malignant tumors—aleukemic and leukemic lymphosarcoma. The classification of the polymorphonuclear leukocyte is similar. Polycythemia vera, leukemic erythrocytoma and aleukemic erythrocytoma are classified as proliferations of the neoplastic type of the red blood corpuscle. Gaucher's disease and Niemann-Pick disease are placed in the class of reactive hyperplasias of the reticulum cell. Hodgkin's disease is divided into a local and a generalized form. Some patients with Hodgkin's disease present definite malignant characters, and the condition may be termed Hodgkin's sarcoma.

MOORE, New York.

STUDIES ON THE MYOCARDIAL ASCHOFF BODY: I. DESCRIPTIVE CLASSIFICATION OF LESIONS. LOUIS GROSS and JOSEPH C. EHRLICH, Am. J. Path. **10**:467 (July) 1934.

An excellent review of the literature is given, with credit to Goodhart (*Tr. Path. Soc. London*, 1879) for the first report of the Aschoff body. On the basis

of seventy uncomplicated cases of rheumatic fever the authors attempt to classify the histologic types of the Aschoff body. The type apparently depends on whether it originates from dense or loose collagen, on the phase of the life cycle of the lesion and also to some extent on the individual reaction occurring in the given case. Seven types are differentiated: small cell coronal, large cell coronal, syncytial coronal, reticular, mosaic, polarized and fibrillar. The nodule is generally oval, disklike or spindle-shaped in form, but may be spherical. The detailed description of each type is best read in the original.

MOORE, New York.

STUDIES ON THE MYOCARDIAL ASCHOFF BODY: II. LIFE CYCLE, SITES OF PREDILECTION AND RELATION TO CLINICAL COURSE OF RHEUMATIC FEVER. LOUIS GROSS and JOSEPH C. EHRLICH, Am. J. Path. **10**:489 (July) 1934.

Gross and Ehrlich studied seventy cases of rheumatic fever in which a clinicopathologic correlation could be made and conclude that the Aschoff body has a definite life cycle, which may be divided into three stages. In the earliest phases the small cell coronal and the reticular type are present (see previous paper) up to the fourth week. From the fourth to the thirteenth week the large cell coronal, the syncytial coronal, the mosaic and the large irregular cell polarized types of bodies are noted. From the ninth to the sixteenth week polarized types are present, and finally the fibrillar types appear. The earliest lesions are apparently influenced by the reactivity of the tissue, dependent on the history of a previous attack.

In one hundred and eighty-one hearts showing evidence of rheumatic infection, past or present, Aschoff bodies were found in 59 per cent. However, they were present in 90 per cent of the hearts in cases in which the disease was clinically or pathologically active.

It is suggested that there is a difference in the distribution of the Aschoff bodies in relation to the number of attacks. The interventricular septum and the posterior wall of the left ventricle are most frequently involved.

MOORE, New York.

GLYCOGEN-STORAGE DISEASE. E. M. HUMPHREYS and K. KATO, Am. J. Path. **10**:589, 1934.

Glycogen storage disease (thesaurismosis glycogenica, von Gierke) is a disorder of infancy and childhood, possibly familial, affecting both sexes. It is characterized anatomically by enlargement of organs and the storage of glycogen chiefly, but not exclusively, in the enlarged organs. Two main types have been delimited, glycogenic hepatomegaly, or hepatonephromegaly, and glycogenic cardiomegaly. The affected organs may attain great size and may contain glycogen in unprecedented amounts. One peculiar feature is delayed postmortem glycogenolysis, and the search for glycogen has been successful in spite of adverse circumstances and imperfect technic. In only a few instances has glycogen storage been associated with degenerative or proliferative changes. At least in the hepatomegalic type, clinical studies have seemed to point to an impairment of the mechanisms concerned in the mobilization of glycogen and the regulation of the blood sugar. Less is known of the cardiomegalic type. We present the clinical and postmortem studies of three proved cases and one probable case of cardiomegalic glycogen storage disease. The weights of the hearts were from 3.3 to 7 times the normal, and the myocardial fibers were enlarged, vacuolated and (in three cases) filled with glycogen. It is probable, though proved in only one case, that the liver and kidneys were affected similarly but to a lesser degree. In two cases the skeletal muscles showed an unusual type of vacuolar degeneration, and in one of these the vacuoles contained much glycogen. This report brings the total number of proved cases to fifteen.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

STATUS LYMPHATICUS. D. SYMMERS, Am. J. Surg. **26**:1, 1934.

Status lymphaticus may be defined as a combination of hereditary constitutional anomalies, entering into which, among other things, are certain peculiarities of configuration with preservation or even hyperplasia of the thymus at an age when involution is to be expected, hyperplasia of the lymphoid cells in the spleen, intestines and elsewhere, changes in the distribution of hair and hypoplasia of the vascular system. Status lymphaticus is compatible with prolonged life, but occasionally it is associated with sudden death on trivial provocation due, apparently, to anaphylaxis, or to spontaneous rupture following increased intracranial pressure acting on a congenitally hypoplastic vessel. Status lymphaticus is encountered in about 6.2 per cent of all autopsies. It occurs in males six times oftener than in females.

FROM THE AUTHOR'S SUMMARY.

SIMULTANEOUS BILATERAL SPONTANEOUS PNEUMOTHORAX: A REVIEW OF THE LITERATURE AND REPORT OF A RECURRENT CASE DUE TO CONGENITAL CYSTS OF THE LUNGS. WALDO R. OECHSLI and SETH H. MILES, Tubercle **15**:402 (June) 1934; also, Am. Rev. Tuberc. **30**:239 (Sept.) 1934.

The commonest causes of the reported cases of bilateral spontaneous pneumothorax are pulmonary tuberculosis (51 per cent), an idiopathic condition (21 per cent) and emphysema (13 per cent). The authors report a case due to congenital cystic disease of the lungs in which bilateral collapse occurred twice and unilateral collapse once, with complete reexpansion in each instance. Death occurred from cardiac failure due to the extensive cystic disease of the lungs. Associated congenital anomalies were hypopituitarism with typical Fröhlich's syndrome, diabetes insipidus and hypothyroidism.

In the diagnosis of cystic disease of the lung the roentgen rays are most to be depended on. Large isolated cysts cause clearcut annular shadows with no perifocal reaction. Smaller cysts may be difficult to demonstrate, but when there is free communication with the bronchi iodized oil may be of considerable help. When communication is blocked the cysts appear on the film as circular opacities. Even in the presence of extensive cystic changes patients may be practically free from symptoms. Superimposed infection or, as in this case, pneumothorax may bring the condition to the attention of the physician.

EUGENE SMITH, Ogden, Utah.

THE DIABETIC CHILD; ETIOLOGIC FACTORS. HENRY J. JOHN, Ann. Int. Med. **8**: 198 (Aug.) 1934.

This article stresses the hereditary factor in the causation of diabetes in children and points out that the disease is transmitted as a recessive character according to the mendelian law. The birth of future diabetic persons should be prevented by advising against marriage, not only among persons with diabetes but among those with a family history of diabetes. A study of nineteen pairs of twins reported in the literature further illustrates the hereditary nature of diabetes.

The opinion is expressed that, contrary to general belief, infections play an important rôle in the development of diabetes in children, and that during and following acute infections children should have a weekly urinalysis to detect the onset of diabetes. Obesity in the child is of minor importance as an etiologic factor in the production of diabetes. A group of obese children showed three times the resistance to diabetes that a group of obese adults possessed. Arteriosclerosis and hyperthyroidism likewise are of little etiologic importance. Syphilis has no part in the causation of this disease.

READING, Galveston, Texas.

THE MONOCYTE, MONOCYTOSIS, AND MONOCYTIC LEUKOSIS: A CLINICAL AND PATHOLOGICAL STUDY. CHARLES A. DOAN and B. K. WISEMAN, Ann. Int. Med. **8**:383 (Oct.) 1934.

In a careful and complete study Doan and Wiseman present data which indicate that the monocyte is a distinct cell entity with a characteristic function and life

cycle. In discussing the monocyte in pathologic states they point out that absolute monocytosis in the blood in tuberculosis is indicative of the progressive formation of new tubercles in the tissues. The monocyte of the blood is identical with the monocyte of the tissues, and its increase in the blood results from proliferative activity of these elements in the body as a whole. The stimuli responsible for monocytic proliferation are the lipoids, more particularly, the tuberculophosphatids.

Among seventy-six cases of leukemia studied the monocytic form of leukemia occurred in about 16 per cent or less, while the myeloid type accounted for 37 per cent and the lymphocytic for 47 per cent. The age incidence ranged from 4 to 70 years.

In other pathologic states, namely, Hodgkin's disease, syphilis, pneumonia and the xanthomatoses, the proper evaluation of the monocyte may possibly be of value in the management and diagnosis. Chronic monocytic leukemia and the problem of mixed leukemia are also discussed.

READING, Galveston, Texas.

ADVANTAGES OF PRE-OPERATIVE X-RAY IN KIDNEY TUMOR IN CHILDREN. ALEXANDER RANDALL, Ann. Surg. **100**:462 (Sept.) 1934.

The prognosis of tumor of the kidney has always been bad, and it is especially bad in children because the paucity of urinary symptoms and the absence of characteristic pain render early diagnosis impossible, and so most tumors are treated as advanced lesions. These malignant renal tumors of childhood are distinct from the tumors of adult life. They are essentially embryonic tumors and are always characterized by a multiplicity of tissue elements.

Roentgen therapy has been found to produce a marked diminution in the size of the tumor, but experience has shown that the therapy is not completely curative, and recurrences follow which offer increased resistance to irradiation. The author decided to use the roentgen rays as a preoperative measure, and during the stage of improvement (from the fourth to the sixth week after irradiation) do a nephrectomy as radical as possible.

The cases of three patients aged 6, 10 and 3 years, respectively, are reported in detail.

BANTIN, Omaha.

SPLENECTOMY IN MOTHER AND DAUGHTER FOR FAMILIAL HAEMOLYTIC JAUNDICE. FREDERICK A. LOOP, Ann. Surg. **100**:518 (Sept.) 1934.

Hemolytic jaundice may be defined as a chronic hemolytic disease, either familial or acquired, characterized by splenomegaly, varying degrees of secondary anemia, a typical blood picture and the occurrence of acute exacerbation with hemolytic crises. The etiology is unknown, and the primary cause is probably not in the spleen. The rationale of splenectomy is the removal of a scavenger which preys on red cells of increased fragility. The value of splenectomy for hemolytic jaundice has been proved. The procedure may be considered almost specific.

Loop presents two case reports of familial hemolytic jaundice in which splenectomy had been done on mother and daughter.

BANTIN, Omaha.

BLUE SCLEROTICS, FRAGILE BONES AND DEAFNESS. JOSEPH DESSOFF, Arch. Ophth. **12**:60 (July) 1934.

The familial nature and close association of blue sclerotics, fragility of the bones and deafness have been noted and commented on for years, although no satisfactory explanation has been given for all the phenomena. The blueness of the sclera has been attributed to the thinness of that structure, revealing the choroidal pigmentation, or to a lack of lime salts in the connective tissue of the sclera. Sixty per cent of patients with blue scleras are subject to fracture, which may be present at birth or occur when the child begins to walk or even in adult life. Deafness manifests itself after the age of 20. Only recently has this feature of the syndrome been observed as a part of the picture, and it is attributed to otosclerosis.

Heredity is a prominent feature, the disease being transmitted by affected parents to their children. Dessoff reports a case of blue scleras, susceptibility to fracture and kerato-iritis with megalocornea and keratoconus without glaucoma.

WESCOTT, Chicago.

CHRONIC ADHESIVE PERICARDITIS IN CHILDREN AND ITS SURGICAL TREATMENT: I. JACOB L. ROTHSTEIN, Arch. Pediat. **51**:219 (April) 1934.

In prepartion for the report of a case of Pick's disease, or pericarditic pseudocirrhosis of the liver, at a later date a general consideration of chronic adhesive pericarditis is given. This entity frequently produces no signs or symptoms referable to the heart, but when the filling of the heart during diastole is hindered diagnosis can be made, and surgical intervention is frequently advisable. Pick's disease is a symptom complex due to the pericardial pathologic changes. Any acute pericarditis, due either to blood-borne organisms or to direct extension from neighboring foci of infection, may become adhesive. Rheumatic, tuberculous and pyogenic inflammations of the pericardial sac are the most common. Traumatic hemopericardium may later give rise to adhesive changes. Chronic adhesive pericarditis can be divided into two groups: first, mediastinopericarditis, characterized by adhesions between parietal pericardium and either the mediastinal structures or the diaphragm or both and, second, the "concretiopericardii" type with adherence of the two layers of the pericardium and encasement of the heart in an inelastic, firm envelop of scar tissue. The symptoms, of course, will depend on the degree of contraction of the scarred pericardium. When the heart is embarrassed by a throttling contracted scar, it is not surprising to find hepatic changes and filling of serous cavities with fluid. This condition constitutes the entity Pick's disease, which was described by this investigator in 1896.

Congestion of the hepatic structure results in the formation of fibrosis and a pseudocirrhosis and likewise produces serous effusions. The symptoms of this lesion include dyspnea, abdominal discomfort and ascites. The signs are, briefly, cardiac enlargement, fixation of the heart, ascites without extremital edema, Broadbent's retraction of the interspaces, pulsus paradoxus, calcification of the pericardium (seen with the roentgen rays), increased venous pressure, friction sounds over the pericardial region and fixation of the electrical axis in the electrocardiogram. Fluoroscopic examination may reveal a rising of the heart with the wall of the chest on inspiration, rather than the normal fall with the diaphragm. This sign was discussed by Holmes. The treatment of Pick's disease may be classified as (1) conservative or medical and (2) radical or surgical. The first involves restriction of activity, digitalization, the administration of diuretics and the mechanical removal of accumulated fluids. The latter involves either the Brauer cardiolysis operation, wherein the heart is freed by resection of ribs and a cartilaginous portion of the sternum, or the Delorme decortication procedure, wherein the constricting pericardium is actually cut away from the surface of the heart and the great vessels. The latter method seems to be the procedure of choice. Care must be taken in this method to remove the scar tissue from the left ventricle before removing it from the right one, else the venous stasis may be transferred from the caval system to the lungs and disaster result.

WADDELL JR., University, Va.

ERYTHROCYTE SEDIMENTATION RATE IN RHEUMATIC INFECTION. H. WILLIAM ELGHAMMER, Arch. Pediat. **51**:281 (May) 1934.

The Linzenmeier-Raunert micromethod of the sedimentation test was used as a routine measure in the cases of one hundred and seventy-one children convalescing from rheumatic fever. These children were followed for a period of ten months. The total number of observations was 1,143, with an average of from five to fourteen weekly readings in each case. It is believed that the sedimentation test furnishes a reliable indication in regard to the activity of rheumatic infection,

when clinical manifestations of activity are not present. Uncomplicated chorea did not cause an increase in the sedimentation rate, suggesting that chorea is an expression of previous damage from rheumatic infection, or that the disease may not be of rheumatic origin. A study of the sedimentation rate following tonsillectomy seemed to prove activities of the infection as the result of operation. The test furthermore appeared to give valuable information regarding the progress and prognosis. A persistently high sedimentation rate was present in the cases that proved fatal, while a low rate coincided with clinical improvement. In chronic valvular disease with considerable damage, decompensation did not take place as long as the rate remained low.

WADDELL JR., University, Va.

CHRONIC ADHESIVE PERICARDITIS IN CHILDREN AND ITS SURGICAL TREATMENT: II. JACOB L. ROTHSTEIN, Arch. Pediat. **51**:288 (May) 1934.

A case of Pick's disease occurring in a 12 year old boy is reported in detail. Abstracts taken from the literature of reports of thirty-four cases in which operation for chronic adhesive pericarditis was performed on children 15 years or younger are tabulated, with an analysis of the symptoms, signs and results. A previous article by the author on the same subject has been published in the preceding issue of the *Archives of Pediatrics*. Both articles are valuable contributions to the pediatric literature and should be read in their entirety, since they do not lend themselves to suitable abstracting.

WADDELL JR., University, Va.

HODGKIN'S DISEASE IN CHILDREN. IRA I. KAPLAN, Arch. Pediat. **51**:325 (May) 1934.

Hodgkin's disease is not uncommon among children and may be associated with tuberculosis. It is manifested most often in children by swelling of the lymph nodes in the neck. This may be an indication, as Symmers suggests, of the advanced stage of the disease. It occurs most frequently in males. Biopsy should be done in all cases to verify the diagnosis. The only effective treatment is roentgen therapy, which was the procedure employed in all the cases herein reported. The prognosis in all cases is serious, and in most instances the condition is rapidly fatal.

AUTHOR'S CONCLUSIONS.

ALLERGIC MANIFESTATION IN INFANCY. W. C. SERVICE, Arch. Pediat. **51**:383 (June) 1934.

While hay fever and asthma may occur in infancy they are not as common as vasomotor rhinitis or bronchitis. Service believes that sensitization of the gastrointestinal tract may be of rather common occurrence. Sensitization in this area may be manifested by vomiting, severe cramps, diarrhea or vague symptoms, such as lack of appetite, abdominal discomfort or malnutrition. It is thought that in many such cases probably no diagnosis is made. In certain cases spasm of the pylorus and colon may have an allergic basis. Suggestions as to diagnosis and treatment are given.

WADDELL JR., University, Va.

THE ALLERGIC NATURE OF THE INFANTILE DIATHESES AND ASSOCIATED FREQUENCY OF A WIDENED MEDIASTINAL SHADOW (THYMUS). I. HARRISON TUMPEER, Arch. Pediat. **51**:407 (July) 1934.

The title of the new specialty, allergy, and the anticipation of its two chief technics, namely, the scratch test of von Pirquet and the intradermal test of Schick, are singularly pediatric.

Tumpeer tabulates certain signs and symptoms occurring in infancy and early childhood which he believes are allergic in nature and points out the similarity of these signs to certain features of the so-called infantile diatheses. It is thought that the pictures described under infantile diatheses are but fragments of the larger puzzle of allergy.

WADDELL JR., University, Va.

DETERMINING THE INFECTING ORGANISM IN SYSTEMIC DISEASE IN CHILDREN. MYER SOLIS-COHEN, Arch. Pediat. **51**:419 (July) 1934.

Solis-Cohen calls attention to the frequent failure of the so-called removal of foci of infection to cure systemic disease and attributes this lack of cure in many instances to the common misconception of focal infection, which concentrates attention on infected tissue rather than on the infecting agent. Removal of certain infected tissue does not remove infecting germs from neighboring tissue. It is believed that the only means of overcoming persisting infection is through the patient's defensive forces aided by hygienic measures and proper vaccine therapy. Since the failure of vaccine therapy is frequently due to improperly prepared vaccine or to vaccine lacking the necessary antigen, Solis-Cohen strongly advises a pathogen-selective culture from which vaccine is prepared. An analysis is presented of one hundred and twenty-one pathogen-selective cultures in children taken in a hospital ward over a period of fourteen years.

The intracutaneous test is thought to be a reliable one for hypersensitiveness to bacterial endogenous and exogenous toxins, and the scratch test is condemned.

WADDELL JR., University, Va.

DAILY FLUCTUATIONS IN URINARY p_H. FANNY KENYON, CHARLES A. WILSON and ICIE G. MACY, Arch. Pediat. **51**:490 (Aug.) 1934.

"As a part of a series of studies on the alleged metabolic periodicities and their resultant normal physiological range of variations occurring in the body fluids during the 24-hour day and the significance thereof, the p_H values on hourly specimens of urine collected under carefully controlled conditions of a group of mature women and runabout children have been determined.

"1. One hundred and twelve complete 24-hour specimens of urine from 104 runabout boys and girls, ranging from 3 to 15 years of age, and 10 like specimens from 7 women were collected and the p_H value determined at hourly intervals during the waking day and on the composite sample collected after the sleeping period. The fluctuation of urinary p_H for the children ranged from 4.8 to 8.4 and averaged 6.0 for the entire group, the averaged minimum and maximum values being 5.4 and 7.0, respectively, while for the women they ranged from 5.0 to 7.9 p_H.

"2. One child was studied for 9 consecutive days during which she showed as great a fluctuation of urinary p_H as was reflected by the entire group of children.

"3. Alkaline trends were demonstrated after each meal, but definite alkaline tides appeared in the afternoon following the heavy noonday meal for the children and after breakfast for the women.

"4. Individuals not only show extensive variations in urinary p_H through the day, but widely different positions in the p_H range, and this position may change from day to day depending upon many intrinsic and extrinsic factors.

"5. No correlations were found between urinary p_H, volume and specific gravity; emotional excitability; incidence of dental caries; nor between volume of urine and daily temperature and humidity."

WADDELL JR. University, Va.

UROBILIN EXCRETION OF INFANCY AND CHILDHOOD; RELATION TO BLOOD DESTRUCTION AND FORMATION. HUGH W. JOSEPHS, Bull. Johns Hopkins Hosp. **55**:154 (Aug.) 1934.

Although variations in urobilin excretion have for a long time been considered as measuring changes in the rate of blood destruction, it is only recently that there has been any quantitative expression of the relationship of urobilin excretion to blood destruction. This has taken the form of a ratio between the daily urobilin excretion and the total hemoglobin of the body. In this paper the relative constancy of this ratio at different ages has been demonstrated. Certain factors influencing the ratio have been discussed.

1. The ratio tends to be slightly higher in the first two years of life than later in the childhood. 2. An increase during pneumonia is followed by subnormal values which last for a short time early in convalescence. 3. Stimulation of the hematopoietic tissue by iron is accompanied in the majority of cases by an increase in urobilin-hemoglobin ratios. In one case liver also caused a rise in urobilin excretion accompanying stimulation of blood-forming tissue. It was suggested that these stimulants might affect the total metabolism of the blood, not merely the anabolic constituent.

AUTHOR'S SUMMARY.

THE PRODUCTION OF TESTICULAR DESCENT WITH THE WATER-SOLUBLE (ANTERIOR PITUITARY-LIKE) FRACTION OF PREGNANCY URINE. H. S. RUBENSTEIN, Endocrinology **18**:475 (July-Aug.) 1934.

A boy 10½ years old with dystrophia adiposogenitalis, in whom the testicles were still bilaterally intra-abdominal, was treated with daily intramuscular injections of the water-soluble fraction of urine of pregnant women in doses increasing to 250 rat units. After six injections both testes had entered the inguinal canal and with pressure could be made to descend into the scrotum. After five months' treatment, including the addition of thyroid and solution of pituitary, the child's appearance was greatly improved and the genitalia had increased in size.

Experimental confirmation of this result was obtained on six rats treated with the same hormone, litter-mates being used as controls. Testicular descent in the test rats, regardless of their ages, occurred within from three to five days after the beginning of the treatment, while in the control animals descent occurred between 40 and 50 days of age. Although the seminal vesicles were enlarged, no spermatozoa were obtainable.

JACOBSEN, Buffalo.

NEGATIVE EFFECT OF PROLONGED ADMINISTRATION OF OVARIAN SUBSTANCES ON HEMOPHILIA. R. P. STETSON, C. E. FORKNER, W. B. CHEW and M. L. RICH, J. A. M. A. **102**:1122 (April 7) 1934.

Large amounts of several ovarian substances were given to seven patients with hemophilia over periods of from twenty-eight to eighty-one days. Observations of the coagulation time of the blood showed that in no instance could it be depressed by such therapy. Theelin administered subcutaneously to two patients for from three to seven days neither reduced the clotting time nor stopped the bleeding. No clinical improvement was noted which could be attributed to ovarian therapy. In four patients hemarthrosis developed without apparent trauma late in the course of treatment.

BONAR, Salt Lake City.

PORTAL CIRRHOSIS IN A CHILD. M. NORDLAND and L. M. LARSON, J. A. M. A. **102**:1471 (May 5) 1934.

A child of 6 years suffering from portal cirrhosis of the Laënnec type submitted to a Talma-Morison omentopexy. Decompression of the portal hypertension by shunting blood from this system to the systemic circulation relieved the ascites, jaundice and glycosuria and led to a decrease in evidences of collateral circulation. During the two years that the patient lived symptomatic relief was complete.

BONAR, Salt Lake City.

MORQUIO'S DISEASE. D. B. DAVIS and F. P. CURRIER, J. A. M. A. **102**:2173 (June 30) 1934.

Davis and Currier report two cases of Morquio's disease in brothers aged 6 and 9 years. Besides the characteristic osseous dystrophy affecting the trunk and extremities there were extensive changes of the skull, resulting in brain disturbance and optic atrophy. The changes consisted of thinning of the bones of the large skull cap and dilated diploic channels. There were fusion of the sagittal and

lambdoid sutures in both patients and diastasis of the coronal suture in one. These cases are probably the only reported cases with skull manifestations.

BONAR, Salt Lake City.

STUDIES ON POLLEN AND POLLEN EXTRACTS: XII. ENZYME DIGESTION OF POLLEN ALLERGENS. MARJORIE B. MOORE and LEON UNGER, J. Allergy **5**:338 (May) 1934.

Extracts of timothy and also ragweed pollen were digested by pepsin and papain. The skins of normal and of sensitive persons were tested with the resultant preparation. The authors conclude that pollen allergen is a protein or protein-like substance susceptible to hydrolysis by ordinary proteolytic enzymes.

HOYER, Cincinnati.

ANTIBODY RESPONSES IN INFECTIOUS MONONUCLEOSIS. ALAN BERNSTEIN, J. Clin. Investigation **13**:419 (May) 1934.

The blood serums of 300 adult hospital patients were tested for the presence of agglutinins for sheep's red blood cells. In this control group the agglutination titer never exceeded 1:16. In 13 of 15 patients with accepted cases of infectious mononucleosis studied in the acute stage of the disease, the agglutination titer was increased, reaching as high as 1:4,096. The agglutination titer was also found to be increased in persons who had received injections of horse serum, and in two patients who presented doubtful evidence of infectious mononucleosis.

GUEST, Cincinnati.

THYMIC DANGERS. ROY E. DE LA HOUSSAYE, South. M. J. **27**:694 (Aug.) 1934.

The author is convinced that at times a large thymus constitutes a real danger to an infant. He reports several cases illustrating his point.

Both radium treatment and roentgen ray treatment are advocated to reduce the size of the thymus, but the author prefers the use of radium. It is easily placed and retained in the desired location without producing alarm or discomfort in the patient. Radium should be kept at the selected skin distance or the dosage will be entirely different from that desired. Very small changes in this distance make considerable difference in the dosage. The practice occasionally followed of rolling the radium up in a piece of gauze as an applicator is dangerous and cannot be condemned too strongly. It is important that the radium applicator should be covered on the upper surface with lead, because it goes high up under the baby's chin and is apt to produce a burn. No one should attempt to use radium unless he is thoroughly familiar with it.

SCHLUTZ, Chicago.

INFLUENZA. DAVID THOMSON and ROBERT THOMSON, Ann. Pickett-Thomson Research Lab. **9**:1 (Dec.) 1933; **10**:641 (May) 1934.

Two monographs on influenza, consisting of 1,157 pages, are the last of the publications from the pens of David and Robert Thomson that they intend to issue for a few years to come.

The subject of influenza is covered in every detail, from the experimental as well as the practical side, making these volumes greatly important to the research worker and to the practicing physician, who will find all the information that he desires on treatment and other aspects. Should the latter desire to delve into the whys and wherefores of the more abstruse problems of the infection, he will find the information that he seeks stripped of the many technical details that sometimes confuse. They are easy to read and to comprehend. Nowhere in any language is there collected together in so small a space the massive amount of information contained in these books, and the data are complete up to 1934.

Several references were taken at random and checked for accuracy and were found to be painstakingly exact. Most important of all is the fact that the authors' own vast experience gives them an opportunity to valuate the literature critically.

Every angle is considered—the rôles of the various organisms, a historical review, the disease in animals, the epidemiology, complications, treatment, the use of vaccines and serums, etc. In addition, twenty-eight plates give valuable bacteriologic data.

The reviewer recommends these volumes to every practicing pediatrician.

TOOMEY, Cleveland.

STOMATITIS. A. L. SPENCER-PAYNE, Practitioner **132**:671 (June) 1934.

Inflammation of the oral mucosa is almost always an infective process. Its prevention is dependent on an intact mucous membrane and the resistance of the individual. The types discussed in this paper include the following: catarrhal, follicular, aphthous, parasitic, ulcerative, gangrenous and that due to drugs.

A good description of the symptomatology, pathology and treatment is given. Considerable space is devoted to ulcerative stomatitis, or Vincent's disease, and the author lays emphasis on the chronic character of the disease, its contagious nature and the extreme importance of thoroughness in treatment. There is an excellent account of the drugs used.

SAPPINGTON, San Francisco.

"ESSENTIAL" HAEMORRHAGIC PURPURA, WITH TRANSIENT MID-BRAIN SYMPTOMS. H. A. DUNLOP, Practitioner **132**:709 (June) 1934.

Dunlop presents in detail the case history of a 10 year old girl showing the interesting picture of symptoms due to disturbance in the midbrain during the active stage of the purpura. The patient was observed over a period of fourteen months, and seven months after splenectomy she continued to show satisfactory results.

SAPPINGTON, San Francisco.

TETANUS WITHOUT DISCERNIBLE WOUND IN A BABY OF NINE MONTHS. G. SCHREIBER, Arch. de méd. d. enf. **37**:410 (July) 1934.

It is excessively rare to encounter a case of genuine tetanus without visible cause in an infant past the neonatal period. Schreiber reports such an instance in a male child of 9 months. The baby was brought to the hospital (Paris) with a history of convulsions beginning the day before; up to this time he had enjoyed excellent health. These convulsions continued; they were generalized, and between the crises there was great difficulty in nursing, similar to that noted with spasm of the glottis. No abrasion or wound of any sort could be detected, and a tentative diagnosis of eclamptic tetany of the pseudotetanus form was made. The usual measures, such as the administration of chloral and bromides and inhalations of ether, failed to benefit, and lumbar puncture was practiced; this also failed to ameliorate the symptoms. The seizures continued, and the rigidity increased. Finally, on the ninth day, intensive antitetanic treatment was instituted as a last resort and in spite of the history; for ten days 20,000 units of serum was injected subcutaneously each day—a total of 200,000 units. On the fourth day of serotherapy the course of the disease was complicated by two attacks of suppurative otitis media, which yielded promptly to paracentesis. One month after the onset the infant was discharged recovered, with the etiology of the infection unexplained.

AMESSE, Denver.

CHRONIC ATTENUATED SEPTICEMIAS YIELDING TO TREATMENT. RENÉ VINCENT, Progrès méd., July 21, 1934, p. 1177.

The author calls attention to the frequency of gingivitis in patients presenting the symptoms of chronic infection. He believes that in such cases there is evidence

of an infection of the blood stream which may present serious exacerbations and reports good results from treatment with autogenous vaccine, the organism having been obtained from blood from the gums.

LESLIE, Evanston, Ill.

FUTURE OF CHILDREN WITH CELIAC DISEASE. M. SCHACHTER, Progrès méd., July 21, 1934, p. 1187.

Schachter reviews the literature, paying particular attention to the report of M. W. Courtin in 1933. The mortality of subjects who have had celiac disease is high—from 10 to 20 per cent. In those surviving the characteristic of the large abdomen is retained usually until after puberty; in adult life the subjects are rarely robust, and a great number show infantile sex organs with slightly developed secondary sex characteristics. Most patients present some diarrhea, steatorrhea and disturbances of calcium metabolism. They seem, however, to have achieved tolerance for a normal alimentary regimen.

LESLIE, Evanston, Ill.

GASTRIC ULCER IN THE CHILD. H. ROCHER, Rev. franç. de pédiat. **10**:218, 1934.

Rocher reports two cases of gastric ulcer, one in a boy 14 years old, in whom perforation took place before a diagnosis was made, and the other in a boy 8 years old, who for four years had suffered from abdominal pain which occurred often in the middle of the night, constipation, regurgitation and progressive malnutrition. Operation in the latter case revealed an ulcer on the anterosuperior aspect of the pylorus, with adhesion to the gallbladder. Gastro-enterostomy was performed, and the patient made a good recovery. A discussion of the literature follows the report of the cases.

LESLIE, Evanston, Ill.

USE OF THE METABOLISM OF HEMOGLOBIN IN THE STUDY OF BLOOD PATHOLOGY IN CHILDREN AND OF THE ACTION OF LIVER THERAPY. V. F. MADON, Riv. di. clin. pediat. **32**:660 (June) 1934.

The determination of bilinogenic pigment in the feces is very useful in the diagnosis and prognosis for patients with anemia. A patient with chlorosis showed diminished excretion of bilinogenic pigment, while two patients with pseudochlorosis-anemia of the hemolytic type showed markedly increased excretion of bilinogenic pigment. Liver therapy was found by this method to be fundamentally antihemolytic in some cases of anemia and hematogenetic in others.

HIGGINS, Boston.

COEXISTENCE OF CONGENITAL PORPHYRINURIA AND HEMOLYTIC ICTERUS; TREATMENT BY SPLENECTOMY. LUIS DE MARVEL and RODOLFO PONS, Arch. argent. de pediat. **5**:220 (April) 1934.

This rare combination of disorders occurred in a child aged 5 years. Icteric discoloration of the skin had existed since infancy. At the age of 2 years a vesiculobullous eruption appeared on the face, the hands and the legs, which eventually became pustular and resembled the lesions of variola. The eruption periodically disappeared and reappeared. Enlargement of the liver and spleen had existed since birth. Spectroscopic examination of the urine showed the presence of uroporphyrin, and the clinical and blood findings demonstrated the presence of hemolytic icterus. Splenectomy relieved the symptoms of the hemolytic icterus and caused the disappearance of the chronic cutaneous lesions, but there was no change or improvement in the porphyruria.

SCHLUTZ, Chicago.

PNEUMOCOCCIC PERITONITIS IN THE CHILD. CARLOS URRUTIA, Rev. chilena de pediat. **5**:295 (June) 1934.

The author believes that surgical intervention is indicated in every case of pneumococcic peritonitis. It makes the diagnosis certain. The hope that the

peritonitis may become encysted is fallacious. This is the exception rather than the rule. The high mortality following operation reported by many authors is, in the opinion of Urrutia, probably due to a concomitant septicemia. The use of antipneumococcic serum in the postoperative stage is important and is systematically practiced by the author. It invariably seems to improve the condition.

SCHLUTZ, Chicago.

DIABETES INSIPIDA. JULIO DANERI, Rev. chilena de pediat. **5**:306 (June) 1934.

The author states that diabetes is probably produced by a lesion in the posterior lobe of the hypophysis or a lesion in the region of the tuber cinereum. The regulatory center for the metabolism of water seems to be in this region. Syphilis can cause these symptoms. This condition responds well to treatment. Surgical treatment is indicated if the condition is due to a neoplasm. The author also recommends the injection of extract of the posterior lobe of the hypophysis, a salt-free diet to allay the thirst and liberal use of ripe raw bananas.

SCHLUTZ, Chicago.

BONE MARROW PUNCTURE AND THE BLOOD PICTURE IN VISCERAL LEISHMANIASIS IN CHILDHOOD. I. A. KASSIRSKY, Folia haemat. **51**:352, 1934.

Kassirsky diagnoses leishmaniasis, as well as malaria and sepsis, by means of a simplified technic for obtaining bone marrow by puncture of the sternum. In only three of sixty cases has he failed to find Leishman-Donovan bodies. Other methods of diagnosis (lymph node puncture, blood culture, serologic reaction) do not show so high a percentage of positive results. Leishman-Donovan bodies were found on the tenth to the twelfth day of the disease and as late as three weeks after the onset. Fewer parasites were found at the beginning than at the height of the disease, and a few parasites were found from four to five months after the onset. A hypochromic anemia develops, with megaloblasts and other early red blood cell forms in the circulation. The white blood count varies from 6,000 to 9,000 cells. The author discusses the origin of the various elements of the blood as determined from studies of the blood, spleen and bone marrow.

MCBRYDE, Durham, N. C.

NEARLY COMPLETE PYLORIC STENOSIS IN A FIFTEEN YEAR OLD GIRL. J. BECKER, Med. Klin. **30**:968 (July 20) 1934.

Three months before operation the patient began to have pain in the abdomen, vomiting, sour eructations and distention. These symptoms were progressive, and she lost weight. Roentgenograms taken after a contrast medium had been given showed almost complete obstruction at the pylorus. At operation her stomach was found to be enlarged, hypertrophied and blocked at the pylorus by a tumor which was diagnosed ulcus callosum.

DOOLEY, New York.

THE DEMONSTRATION OF INSULIN IN THE BLOOD THROUGH BLOOD TRANSFUSION; INVESTIGATIONS ON NORMAL AND DIABETIC PERSONS. R. BOLLER, K. UIBERRAK and W. FALTA, Wien. Arch. f. inn. Med. **25**:1 (June) 1934.

Through the blood transfusion method it is possible to demonstrate insulin in the blood of persons with a normal metabolism after a meal rich in carbohydrate. Comparison of these experiments with control experiments in which, under the same conditions, insulin has been given intravenously shows that one deals with only a very small amount of insulin (from 1 to 2 units per hundred cubic centimeters of blood).

In the blood of persons with severe diabetes who are highly sensitive to insulin no insulin is found after a test meal. In persons with severe diabetes who are

resistant to insulin the blood shows only slight hypoglycemic characteristics after a test meal. Sometimes the blood sugar is found to be increased in the recipient.

SCHLUTZ, Chicago.

BLOOD TRANSFUSION IN SEPTIC ILLNESSES. ERNST KUTSCHA-LISSBERG, Wien. klin. Wchnschr. **47**:586 (May 11) 1934.

Kutscha-Lissberg states that in the last eight years the use of blood transfusion has become much more extensive than formerly. Recently favorable experiences have been reported in cases of severe toxic diphtheria, but there is no unified point of view with regard to the effect of transfusion in septic illnesses. Hoche reported forty-eight blood transfusions in thirty-three patients suffering from sepsis, with a mortality of 47 per cent. He distinguished between cases of acute and chronic sepsis and found that transfusions were about eight times more favorable in chronic than in acute sepsis. The author points out that comparison of the statistics presumes that sepsis is uniformly defined. He considers sepsis an illness with persistent positive bacterial findings in the blood without provable localization of infection. He reports seventy blood transfusions in forty-five patients with septic illness, of whom twenty-eight were cured and seventeen died, a mortality of 36 per cent.

Some of these patients suffered from puerperal sepsis or sepsis in connection with abortion, others from sepsis in connection with osteomyelitis, fractures, empyema, phlegmon, suppurative arthritis, peritonitis, abdominal phlegmon, pyelitis and mastitis. In most cases too much was expected from a single transfusion. The author believes that repeated transfusions might have cured some of the patients. He believes that the application of blood transfusions in septic illnesses is justified, even though in certain illnesses, such as septic abortion, it is not always satisfactory.

ABT, Chicago.

Nervous Diseases

THE DRAMA IN THE HOME AS SEEN BY THE PSYCHOANALYST. BERTRAND S. FROHMAN, Arch. Pediat. **51**:329 (May) 1934.

Not abstracted.

WADDELL JR., University, Va.

THE TREATMENT OF CHOREA WITH PHENYL-ETHYL-HYDANTOIN. I. B. SILBER and J. W. EPSTEIN, Arch. Pediat. **51**:373 (June) 1934.

An evaluation of twenty-eight cases of chorea in which the condition was treated with phenyl-ethyl-hydantoin is given. The authors believe that phenyl-ethyl-hydantoin is not a specific for chorea. Forty per cent of the patients treated showed marked improvement, 35 per cent slight improvement and 25 per cent no improvement. Severe chorea seemed to be best suited for this form of therapy, the mild condition being influenced little if any by the drug. It is thought that sickness due to phenyl-ethyl-hydantoin resembles serum sickness. The authors believe that phenyl-ethyl-hydantoin is a fairly safe drug and rather discredit the generally accepted idea that administration in the home is unsafe. In this series the drug did not prevent the occurrence of cardiac complications, nor was there any deleterious effect on already existing cardiac disease.

WADDELL JR., University, Va.

SUBDURAL HEMATOMA IN INFANCY. HARRY E. LEFEVER and GENE B. HABER, Arch. Pediat. **51**:457 (July) 1934.

LeFever and Haber report the successful removal of a subdural hematoma in an 18 day old infant. In addition to reporting their case they discuss the etiology, pathologic picture, symptoms, diagnosis and treatment of subdural hemorrhage and the literature on this subject.

WADDELL JR., University, Va.

NEUROLOGIC ASPECT OF VOLUNTARY, AUTOMATIC AFFECTIVE AND SPONTANEOUS PHENOMENA IN THE INFANT, CHILD AND ADULT. SAMUEL M. WEINGROW, Arch. Pediat. **51**:501 (Aug.) 1934.

Weingrow discusses voluntary and involuntary activities of the infant, the child and the adult in the course of the presentation of cases of patients suffering from vascular, infectious, traumatic and degenerative diseases of the brain. This article does not lend itself to profitable abstracting.

WADDELL JR., University, Va.

CLINICAL FINDINGS IN FUNCTIONAL DISTURBANCES DURING CHILDHOOD. H. A. SLESINGER, Arch. Pediat. **51**:534 (Aug.) 1934.

Slesinger warns against the danger of making invalids of healthy children presenting certain clinical findings which may be functional in nature. The following are listed as the more important of this group of clinical and laboratory findings: (1) underweight, (2) a slight elevation of temperature, (3) physiologic heart murmur, (4) a slight decrease in hemoglobin, (5) functional albuminuria and (6) a positive tuberculin reaction.

WADDELL JR., University, Va.

THE PATHOGENESIS OF ANTERIOR POLIOMYELITIS: A REVIEW. THELMA LOVETT, Internat. Clin. **2**:16 (June) 1934.

There is no generally accepted opinion as to the site of invasion in poliomyelitis. The most support, epidemiological and experimental, has been for the nasopharynx. Sufficient experimental evidence has been given to show that the virus can readily enter through the nasal mucous membrane. Epidemiological and immunologic studies indicate contact and carrier as factors in the spread of the disease. The gastro-intestinal tract as a portal of entry has been much talked of recently, along with general lymphatic hyperplasia, but no convincing evidence has been given for combining the two in a scheme of pathogenesis. The route taken by the virus on its way to the spinal cord has not been finally solved. An understanding of the mode of infection would lead to the framing of measures of prevention that could be expected to control the spread of the disease with reasonable certainty.

MILLER, South Bend, Ind.

AN ANALYSIS OF EIGHTY-EIGHT CASES OF POLIOMYELITIS TREATED IN THE DRINKER RESPIRATOR, WITH A CONTROL SERIES OF SIXTY-EIGHT CASES. JOHN FITCH LANDON, J. Pediat. **5**:1 (July) 1934.

No appreciable difference in the mortality was seen in the group of hospital patients treated in the respirator and those not treated in the respirator. However, of the patients who were treated in the respirator and discharged from the hospital able to breathe spontaneously nearly five times as many were dead at the end of eighteen months as in the comparable control group. Emphysema was usually noted post mortem in those who had been in the respirators, indicating that in this type of treatment damage of lung tissue may occur, with subsequent infection or collapse.

LEMASTER, Evanston, Ill.

SERUM THERAPY IN PREPARALYTIC POLIOMYELITIS. JOHN FITCH LANDON, J. Pediat. **5**:9 (July) 1934.

Among 597 patients with preparalytic poliomyelitis, 118 received convalescent serum; 73 were treated with horse serum, and 396 received no serum treatment. The mortality in the group given convalescent serum was 5.93 per cent; in those treated with horse serum, 8.22 per cent, and in the untreated patients, 3.03 per cent. The severity of the paralysis in the untreated and the treated groups was approximately the same. No positive evidence could be seen to indicate that either convalescent serum or horse serum was of any value in preventing the paralysis or lessening the mortality.

LEMASTER, Evanston, Ill.

THE DIFFERENTIAL DIAGNOSIS OF ACUTE POLIOMYELITIS. JOHN FITCH LANDON, J. Pediat. **5**:16 (July) 1934.

During the epidemic of 1931, eighty-six patients were admitted to the Willard Parker Hospital as having poliomyelitis and discharged after a different diagnosis had been made. Several of these patients had either acute enterocolitis or an infection of the upper respiratory tract. In only a few instances was an increase in cells in the spinal fluid noted. Landon cites reports of cases and discusses the differential diagnosis between poliomyelitis and meningismus, acute rheumatic fever, rheumatic torticollis, sepsis, acute appendicitis, tetanus, peripheral neuritis, trauma, hysteria, facial paralysis and transverse myelitis.

LEMASTER, Evanston, Ill.

SPORADIC POLIOMYELITIS. JOHN FITCH LANDON, J. Pediat. **5**:32 (July) 1934.

Two hundred cases of sporadic poliomyelitis (seen from 1926 to 1932) are compared with the cases of epidemic poliomyelitis seen in 1931 from the following points of view: mortality, symptoms, signs, deaths by day of the disease, the distribution of paralysis and the relation of the presence of ocular signs to mortality. The conclusion is that there is no essential difference between the sporadic and the epidemic form of the disease.

LEMASTER, Evanston, Ill.

OPTICOFACIAL WINKING REFLEX. S. M. WEINGROW, Laryngoscope **44**:577 (July) 1934.

In eliciting the opticofacial reflex (closure of the lids when an object is brought suddenly into the field of vision) for testing unilateral or bilateral impairment or destruction of vision, Weingrow places his hand above, to the side of or below the eyes of the subject and out of his field of vision; then he moves it suddenly across the field of vision, thus causing a sudden closure of both lids. If one eye is shielded by a piece of cardboard and the other eye stimulated, there results a bilateral closure of the lids. The afferent path of this reflex is the same as that of the emergency light reflex, but the efferent path seems to be confined to the facial nerve. Weingrow reports cases in which such impairment was presented, with consequent involvement of the opticofacial reflex, and refers to reports of cases in which the efferent part of the opticofacial reflex arc was involved.

[J. A. M. A.]

SYMPOSIUM ON ANTERIOR POLIOMYELITIS (INFANTILE PARALYSIS). THEODORE S. WILDER, JOHN P. SCOTT, JOSEPH STOKES JR., JULIAN M. LYON and GEORGE WAGONER, M. Clin. North America **18**:1 (July) 1934.

These authors present a concise but comprehensive summary of present-day opinions regarding anterior poliomyelitis under the following headings: (1) etiology, pathology and epidemiology, (2) symptomatology and diagnosis, (3) prophylaxis, (4) treatment and (5) nonsurgical orthopedic treatment.

EUGENE SMITH, Ogden, Utah.

RECURRENT MENINGOCOCCUS MENINGITIS. MARK J. WAKEFIELD, M. Rec. **140**:201 (Aug. 15) 1934.

The case of a boy 7½ years old is reported. On admission he showed all the signs and symptoms of meningococcic meningitis. On the seventh day an apical heart murmur (systolic) developed. On the seventeenth day he was ready for discharge, when sudden headache, vomiting spells and rigidity of the neck developed. He again received serum treatment and was discharged well after thirty-three days in hospital. Six weeks later he was readmitted suffering from another attack, for which he again received serum treatment. He was discharged thirty-six days after admission. A review of the literature of these relapsing or recurrent forms of meningitis, as well as the author's comment and discussion, is given.

WILLIAMSON, New Orleans.

THE SUCCESS AND FAILURE OF SUBNORMAL PROBLEM CHILDREN IN THE COMMUNITY. MYRA E. SHIMBERG and WALLY REICHENBERG, Ment. Hyg. **17**:451 (July) 1933.

In a follow-up study for a five year period of 189 feebleminded adolescents, Schimberg and Reichenberg found that 53 per cent had been definitely successful (working regularly and causing no trouble to the community). Sixty-eight per cent were self-supporting, although the average income was low, $12 a week. The group of persons for whom social-psychiatric recommendations had been carried out showed a 77 per cent rate of success, whereas only 7 per cent of those for whom these recommendations had been ignored made a good social adjustment. Heredity, home conditions, physical make-up, race and the size of the family bore little relationship to the ultimate social outcome. Of those in homes of good economic status 67 per cent succeeded, whereas only 46 per cent coming from poor homes made social adjustments. Those with good personalities and desirable personality traits were more successful than those with personality handicaps. (Of the former group, only 66 per cent succeeded, and of the latter group, 38 per cent.) The factor of supervision is apparently important, since 66 per cent of the adolescents under good supervision made a success, while only 38 per cent of those devoid of any regular supervision succeeded. From this study, it appears that the mentally defective person can be treated so as to become an asset to the community.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

PITRESSIN TEST IN EPILEPSY. A. WILMOT JACOBSEN, New York State J. Med. **34**:506 (June 1) 1934.

The pitressin test for epilepsy is described. Retention of body fluids tends to induce epileptic seizures. The antidiuretic effect of pitressin produces a positive water balance to the extent of increasing the body weight from 3 to 6 per cent. Three hundred cubic centimeters of water is given every two hours, and pitressin is injected every four hours until a positive water balance is established. This procedure is continued until eight or ten injections of pitressin have been given or a convulsion has occurred. The results in forty cases are reported. Jacobsen considers the test reliable.

AIKMAN, Rochester, N. Y.

PRACTICAL CONSIDERATIONS IN THE DIAGNOSIS AND TREATMENT OF POLIOMYELITIS. IRVING J. SANDS, New York State J. Med. **34**:587 (July 1) 1934.

Poliomyelitis should be treated in the hospital. Immune serum is of value if administered early. It may be given intravenously or intramuscularly but never intraspinally. Blood transfusions and intravenous injections of a hypertonic solution of dextrose are of value. The various clinical types of the disease are described.

AIKMAN, Rochester, N. Y.

EPILEPSY OF ALLERGIC ORIGIN. T. WOOD CLARKE, New York State J. Med. **34**:647 (July 15) 1934.

A girl of 10 years of age gave a history of severe epilepsy. Positive skin reactions for cattle hair, cottonseed, radish and cheese were found. The last three were removed from the diet, and the child was given inoculations for cattle hair. Complete recovery occurred. Another allergic girl of 17 years has had but one seizure since allergic treatment.

AIKMAN, Rochester, N. Y.

THE PRODUCTION OF SPECIFIC IMMUNITY IN WHITE MICE BY INTRANASAL INOCULATION WITH ENCEPHALITIS VIRUS (ST. LOUIS TYPE). CHARLES ARMSTRONG, Pub. Health Rep. **49**:959 (Aug. 19) 1934.

Forty-three white mice were inoculated intranasally with encephalitis virus (Freeman strain). Nineteen days later these mice and an equal number of controls

were subjected to an intracerebral injection of about one hundred minimal fatal doses of virus. All the control animals died, while twenty-five of the mice previously immunized intranasally survived. It seems logical to suppose that frequently human beings are immunized against encephalitis virus without recognizable symptoms, as probably occurs also in poliomyelitis.

LeMaster, Evanston, Ill.

The Anatomicophysiologic, Clinical and Etiologic Basis of Mental Hygiene of the Infant. Roma Amyot, Union méd. du Canada **63**:794 (Aug.) 1934.

The normal mental and neurologic development of the infant is reviewed. Amyot considers convulsions in the infant an indication of damage to the brain. The most important causes of such damage are obstetric trauma, infections and syphilis. Infantile convulsions are often the forerunner of epilepsy in adult life. The prognostic worth of these convulsions is in drawing attention to existing conditions which may be otherwise unnoticed and which may yield to treatment.

Daffinee, Boston.

Age and the Emotions. Katherine M. B. Bridges, Union méd. du Canada **63**:878 (Aug.) 1934.

The author traces the normal course of emotional growth through infancy.

Daffinee, Boston.

The Family Factor in Intellectual Retardation of Children. Alexandre Marcotte, Union méd. du Canada **63**:883 (Aug.) 1934.

Marcotte outlines the most important mistakes which ignorant or egotistic parents make in their relations with their children and makes a plea for the education of parents in these vital matters.

Daffinee, Boston.

An Epidemic of Acute Encephalitis in Young Children. A. Macgregor and W. S. Craig, Arch. Dis. Childhood **9**:153 (June) 1934.

The subject of this article is a small outbreak of acute encephalitis in a hospital, affecting four young children, with two deaths. The clinical details are given, together with the results of examination of the blood and cerebrospinal fluid. Autopsies were performed on the two patients who died, and a complete histologic examination was carried out. Attempts were made to transmit the infection to animals. Various possibilities in connection with diagnosis are considered. The observations appear to indicate that the condition most closely resembled the lethargic type of epidemic encephalitis. The children had been in close contact with patients with postencephalitic parkinsonism. The possibility of infection from this source is discussed.

Kelly, Milwaukee.

The Aetiology of Idioglossia. I. J. Wolf, Arch. Dis. Childhood **9**:171 (June) 1934.

Idioglossia is dyslalic speech so extreme that it is incomprehensible to the ordinary listener. It is merely a stage in the development of speech, whether the speech be normal or retarded. Its manifestations are the same as those of universal dyslalia: omission and reduction, reduplication, assimilation, metatheses, etc. Retarded lingual development, of which idioglossia is a manifestation, is due to impaired hearing, mental deficiency, articulatory dyskinesthesia and congenital auditory imperception. The idioglossia in these cases may be termed pathologic idioglossia to distinguish it from the idioglossia of normal speech development, or physiologic idioglossia.

Kelly, Milwaukee.

MENTAL DEFICIENCY AND HEREDITY. F. GRUNDY, Brit. M. J. **1**:1164 (June 30) 1934.

In this article a statistical study of school children and mental defectives, with special reference to the family history, is reported. A summary of the author's conclusions is as follows:

1. Roughly, 75 per cent of defectives of all grades come of stocks which exhibit distinct mental abnormalities, of which deficiency and gross dulness are the commonest.

2. In the remaining 25 per cent, mental abnormalities are attributable to environmental causes in a few cases, but in most cases they are without apparent cause.

3. Feeblemindedness and dulness are familial to a much greater extent than lower grade deficiency.

4. The mating of two mentally defective persons yields offspring who are all defective.

5. The mating of two persons of "poor type" yields offspring of "poor type," who are often defectives in an educational and sometimes in a social sense.

6. "Dull parents, dull children" is the usual association.

7. When a neuropathic stock exists the chance presence of an adverse environment, using the term in its broadest sense, may produce actual deficiency in persons who might not have been defective without the existence of such a factor.

ROYSTER, University, Va.

A SECOND ATTACK OF ACUTE POLIOMYELITIS. THOMAS MOORE, Brit. M. J. **2**:166 (July 28) 1934.

Moore reports the case of a patient who, from the history and physical examination, was supposed to have had an attack of poliomyelitis at 9 months and who had a second attack at 7 years.

ROYSTER, University, Va.

BEHAVIOR DISORDERS IN INFANCY AND CHILDHOOD. G. K. CROSS, South African M. J. **8**:597 (Aug. 25) 1934.

Cross defines behavior disorders as "temporary departures from normal conduct, which are all curable with correct treatment, and in no instance proceed to, or even abut on, insanity."

While it is usually true that nervous parents have emotional children, the opposite is seen often enough to emphasize the importance of environmental factors. The ideal method of investigating behavior disorders requires a pediatrician, psychologist and social worker.

The author discusses in what seems a somewhat disjointed manner many of the factors that may contribute to behavior disturbances. Infections are regarded as important factors, as are habits. For most of the disturbances, such as disorders of sleep, he advocates a rational attitude on the part of the parent, but for masturbation he advocates at first telling the child the act is "wrong and harmful," and if that fails severe whippings are advised.

TENNEY, Madison, Wis.

PSYCHIATRY AND RACE BETTERMENT. E. K. HENDERSON, Tr. Med.-Chir. Soc. Edinburgh, 1934, p. 105; in Edinburgh M. J., August 1934.

Professor Henderson, psychiatrist at the University of Edinburgh and physician-superintendent of the Royal Hospital for Mental and Nervous Diseases, believes in child guidance and psychiatric clinics and departments, both outside and inside the hospital. Care for disordered mental states is needed, as mentally unsound and delinquent persons will continue to appear, coming "within the range of variation just as genius does." But eugenics is necessary, and the medical profession must indorse the right of all persons to enter the world sound and "so surrounded environmentally as to have an equal chance."

The author emphasizes the fact that the figures of Rüdin would be increased greatly if both parents instead of one had certain diseases. If one parent has Huntington's chorea it develops in 50 per cent of the children. In manic-depressive states 33 per cent of children are affected. In schizophrenia and epilepsy mental abnormalities may be expected in 50 per cent of the children. In hysteria from 48 to 61 per cent of the children will have mental and nervous abnormalities.

Henderson discusses the question of sterilization of the unfit, but believes more in a positive program of eugenics. The objection to assortative mating of parents is that "like" tends to marry "like"—defectives wed defectives, the gifted marry those of like quality. The latter group tends to small families. The birth rate is getting lower for parents who should be able to produce the best children. In Scotland the class of miners and craftsmen have an average of seven children per marriage; physicians and lawyers have three. As regards the question of eugenics and race betterment, the author states that there are no doubt many fallacies, and even although "a selector of sufficient knowledge," as Haldane states, "might perhaps obtain from the genus at present available in the human species a race combining an average intellect equal to that of Shakespeare with the stature of Carnera, yet he could not produce a race of angels. For the moral character or for the wings he would have to await or produce suitable mutations."

NEFF, Kansas City, Mo.

DIAGNOSIS OF VASCULAR TUMORS OF THE BRAIN. A. BARSKY, Arch. de méd. d. enf. **37**:45 (July) 1934.

In spite of the remarkable general advance in topical diagnosis, sufficient data are not yet available to enable one to define with any great degree of assurance the exact seat of cerebral tumors in infancy. Especially is this true of neoplasms originating in the choroid plexus, since the signs and symptoms are not local but manifested at a distance following early hypertension of one of the ventricles. The difficulty is further increased through the easy distensibility of the cranial vault in the very young patient. Diagnosis is usually made at autopsy.

Barsky reports the case of a boy of 10 months who was admitted to the hospital at Dniepropetrovsk with a history of attacks of vomiting for the preceding two months; there was an area of softening 3 cm. in diameter in the left parietal region, and the parents reported a sudden increase in the size of the head. On examination the circumference of the skull was 49 cm., while that of the chest was 40 cm.; there was incessant movement of the left arm, and the tension of the fontanel was greatly increased. Ventricular puncture was done, and 75 cc. of sanguineous fluid was withdrawn; the following day a similar amount was obtained by the lumbar route. The Pirquet and Wassermann reactions were negative. The optic nerves were atrophied. During the two weeks' residence in hospital the baby continued to lose weight, in spite of repeated depletion of the cerebrospinal fluid; the vomiting persisted, but there was no febrile response at any time. Death occurred on the fourteenth day. Autopsy revealed a tumor of the left ventricle, 7 by 3.8 by 2.5 cm., attached by two vessels to the choroid plexus. The histologic diagnosis was hemangio-endothelioma.

AMESSE, Denver.

TREATMENT OF CEREBROSPINAL MENINGITIS BY THE SUBOCCIPITAL ROUTE. FACATSELLI and FACATSELLI, Arch. de méd. d. enf. **37**:527 (Sept.) 1934.

Invasions of the epidemic type of cerebrospinal meningitis, which are most resistant to specific treatment and are consequently greatly prolonged, usually belong to the so-called *cloisonné* type in which the orifices of the ventricles are frequently closed and the subarachnoid space partitioned off by strong adhesions. These factors offer such mechanical difficulties to the proper diffusion of meningococcic serum that other methods than the usual lumbar route of injection must be employed. The diagnosis of these closed forms of meningitis is readily made in infants. If spinal puncture shows hypertension, if abundant fluid escapes, and if the fontanel is depressed after such withdrawal, one may conclude that there

is no obstruction. Should the opposite be found, however, it is fair to conclude that the adhesions exist. Among nine cases observed by the authors, two were of the latter variety; in another series of eleven cases there were five showing obstruction. All the patients with the closed cases were treated by the suboccipital, lumbar and intraventricular routes, except those older children in whom the latter method could not be used.

There was recovery in 100 per cent of the patients treated within thirty-six hours from the time of onset; in those seen later in the course of the disease the mortality was 50 per cent. The authors conclude that, as in diphtheria, early and intensive treatment of cerebrospinal meningitis is mandatory.

AMESSE, Denver.

HYDROCEPHALUS WITH GLAUCOMA IN AN INFANT. P. PESME, Arch. d'opht. **51**:524 (Aug.) 1934.

Pesme suggests that this unusual case of hydrocephalus and glaucoma in an infant—ocular and cerebral glaucoma—should draw attention to the relationship which may exist between disturbances of the intracranial tension and the tension of the eye. The case of a child who died at the age of 11 months is fully described from both the clinical and the anatomic standpoint. In view of the known relationship between the retinal circulation and the intracranial pressure he propounds the hypothetic question as to what happens when there is only a partial defect of the normal drainage system of the eye and the brain. He calls attention to the frequency of high myopia in hydrocephalus and Crouzon's disease. The next step is the intimation that myopia may be dependent on mild intracranial hypertension, manifested possibly by the headaches which are of frequent occurrence in progressive myopia.

MARLOW, Syracuse, N. Y. [ARCH. OPHTH.]

JUVENILE CRIMINOLOGY AND INFANTILE MENTAL DEFICIENCY. JACQUES ROUBINOVITCH, Presse méd. **42**:1338 (Aug. 25) 1934.

Roubinovitch presents some statistics from the service for medical and psychologic examination of juvenile delinquents in Paris. He gives detailed figures for the year 1933, when there were 1,133 minors detained, as contrasted with 1,943 in 1928. Of these, 660 were examined. Eighty per cent were from the working classes and 17 per cent from the middle class. Thirty-five per cent were from divided families, that is, families separated by divorce or for other reasons and lacking one or both parents. Alcoholism occurred in 30 per cent of the families.

Among the minors held in the corrective schools of Fresnes, flight was the offense in 49 per cent of the boys. Prostitution was the leading offense among the girls, constituting 78.6 per cent of the offenses. Among these, 32.5 per cent showed signs of tuberculosis; 17 per cent were syphilitic.

From 20 to 22 per cent of all the subjects showed malformations of the head, face, trunk, genitalia or limbs, indicating a degenerated physical heredity. Moral and psychic defects were found in 75 per cent of the boys and 80 per cent of the girls.

Of the boys in detention, 5.3 per cent were completely illiterate; 68 per cent had a primary school certificate, and 3.8 per cent had attended a secondary school. Of the girls, 6.7 per cent were illiterate; 78 per cent could read and write; 14 per cent had a primary school certificate, and 2 per cent had had secondary school work. Figures collected since 1927 show that from 70 to 80 per cent of minor delinquents are of intelligence inferior to the average. They may be considered as pedagogically and morally abandoned. The percentage of delinquency among backward and unstable children educated in the Institute of Asnières, a school provided for children of this type, is less than 1. The solution of the problem of juvenile delinquency, the author insists, lies in placing children found abnormal by neuropsychiatric examination in schools established for the purpose. Laws governing the placing of these children exist in France, but the enforcement is difficult.

BIEKER, St. Petersburg, Fla.

A Case of Simmonds' Disease. Léandre Cervera, Albert Folch and Bonaventura Benaiges, Rev. franç. d'endocrinol. **12**:15 (Feb.) 1934.

The authors report increase in weight and general improvement in the case of a girl, aged 15 years, suffering from Simmonds' disease. The treatment consisted of the application of high voltage roentgen rays to the temporal, occipital and superior parietal regions. The focal distance was 40 cm.; the filter used was 0.005 zinc and 0.002 aluminum; the tension was 120 kilowatts, and the daily dose 150 roentgens. The treatments were given every other day, and the field was regularly changed in order to avoid loss of hair. In addition, the patient was given an extract of the anterior lobe of the pituitary and vitamin therapy.

Notkin, Poughkeepsie, N. Y. [Arch. Neurol. & Psychiat.]

Papillary Stasis in Encephalitis. I. Alfandary and S. Stayitch, Rev. d'oto-neuro-opht. **12**:502 (July-Aug.) 1934.

Papillary stasis may at times accompany encephalitis of any origin, although in such a case it is most often inflammatory papillitis rather than choked disk of mechanical origin. The important differentiation between tumor and encephalitis is sometimes difficult.

A child, aged 10 years, who was admitted to the hospital on Oct. 19, 1933, for two weeks before had had general malaise and latterly vomiting four or five times daily. Suddenly violent headaches occurred and persisted and were followed by epileptic convulsions, fever, a high leukocyte count (from 25,000 to 32,000), amaurosis, a positive Babinski sign and bilateral papillary stasis. The pupils were dilated, but the light reflex persisted. One attack of epilepsy was of the jacksonian type. After a few days the child was taken home, and within a few days the alarming symptoms disappeared. Reexamination ten weeks later showed all in order except a slight temporal pallor of the disks. Infectious meningitis and cerebral tumor could be eliminated. Abscess of the brain appeared probable at one period, and even later the possibility of a latent abscess was entertained. Acute panencephalitis of the Strümpell-Leichtenstern type is the probable diagnosis. Papillary stasis does not always mean increase of intracranial pressure, and still less may one deduce from it indication for surgical intervention.

Dennis, San Diego, Calif. [Arch. Neurol. & Psychiat.]

A Case of Ventricular Hydrocephalus. J. Monforte Portils, An. de pediat. **1**:287 (May) 1934.

The author presents a case of noncommunicating hydrocephalus in which the ventricles are enormously dilated. The spinal fluid pressure was 25 mm., and the ventricular pressure was 45 mm. He discusses the various etiologic factors.

Herron, Spokane, Wash.

Introduction to the General Pathology of the Neuro-Endocrine System. L. V. Cuervo, Arch. de med. inf. **3**:633 (June) 1934.

This article of fifty pages with a bibliography should be read in its entirety by any one interested in the subject. Cuervo concludes that the combined pathologic condition of the glands and of the nervous system constitutes a correlated disorder. One must consider the glands of internal secretion as regulating organs or correlating agents which the organism has assigned to the nervous system for maintaining its unity.

Sanford, Chicago.

A Case of Internal Hydrocephalus. Z. P. Interian, Arch. de med. inf. **3**:711 (June) 1934.

In this child chronic internal hydrocephalus was proved to be of the nonobstructive type by injecting methylthionine chloride (methylene blue), thus showing the

normal circulation of fluid between the ventricular cavities and the subarachnoid spaces. The child's blood and spinal fluid, as well as those of the mother, gave negative Wassermann reactions. In spite of this the author treated the child with repeated lumbar punctures and mercury ointment. There was some improvement.

SANFORD, Chicago.

CONGENITAL CEREBROSPINAL DEGENERATION. NAVANTINO ALVES and ALFONSO LUSTOSA, Movimento pediat. Belo Horizonte **1**:94 (June) 1934.

The authors discuss the relationship between Friedreich's ataxia, spasmodic paraplegia, hereditary cerebellar ataxia and diffuse sclerosis. For the cases they have described they have adopted the term congenital cerebrospinal degeneration as given by Guillain and Mollaret. They describe four brothers who suffered from this condition. The only treatment available is exercise and massage.

SANFORD, Chicago.

CEREBRAL DISTURBANCES IN CHILDHOOD AND THEIR ENCEPHALOGRAPHIC DIAGNOSIS: I. KARL RUPILIUS, Arch. f. Kinderh. **102**:194 (July 31) 1934.

The records of 548 children with organic disease of the brain seen at the children's clinic at Graz during the past fifteen years were studied and the results correlated. The patients were divided into nine groups: acute encephalitis, 63 cases; cerebral palsy (Little's disease, hemiplegia, etc.), 215 cases; feebleminded-ness without paralysis, 106 cases; hydrocephalus, 37 cases; microcephalus, 43 cases; deafness, 24 cases; cerebral syphilis, 30 cases; cerebral tumors, 21 cases, and miscellaneous, 9 cases. A history of difficult labor was obtained for from 20 to 30 per cent of the patients. Among the patients with acute encephalitis 10 per cent had been born prematurely, and among those with Little's disease 34 per cent had been born prematurely. In about two thirds of all the cases there was retarded intelligence. Spastic paralysis occurred in 44 per cent of the patients and flaccid paralysis in 17 per cent. About 25 per cent had convulsions. The observations at autopsy in 60 cases are briefly mentioned. Encephalography was done on 129 patients. A great deal more interesting information was brought out in this study.

LEMASTER, Evanston, Ill.

Diseases of the Eye

TELANGIECTATIC GRANULOMA—BOTRYOMYCOSIS. A. HAGEDOORN, Brit. J. Ophth. **18**:561 (Oct.) 1934.

Hagedoorn describes a case of telangiectatic granuloma of the eyelid occurring in a youth aged about 16 years. The latter received a very superficial injury to the lower lid, and after a week a fleshy tumor developed. A few days later, after slight bleeding, the tumor fell off. There was a recurrence. It was then removed surgically, and again recurred, with repeated hemorrhages. It was again removed and did not recur. It occupied the inner third of the lower lid and extended from the free border of the latter to some distance on the cheek. It had the appearance of a granuloma. It was composed of connective tissue with dense masses of cells, in the midst of which numerous small lumens could be detected in many places, and these occurred also in and near the stalk. The peripheral part of the tumor showed an abundance of smaller and larger vessels with scarcely visible walls spread in a tissue resembling an embryonal vitreous body. The tumor had an epithelial covering. In many places it was superficially ulcerated. Only superficially were there staphylococci in great numbers, often arranged in globular masses. This structure recalls the findings in botryomycosis.

Botryomycosis, chiefly met with in horses and apparently only occasionally occurring in man, is characterized by a chronic inflammatory development of granulation tissue and fistulas, causing tumors or swellings of the affected organ

under the influence either of a special variety of Staphylococcus or of a special reactive condition of the human tissue. Only one case of botryomycosis of the eyelid but a few cases involving other regions of the body are described in the literature.

Telangiectatic granuloma is clinically a rather sharply marked off, not uncommon variety of granuloma in man. The etiology is not sufficiently clear. A personal case involving the eyelid is described, and instances in the literature are collected.

The article is illustrated. ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

A CASE OF SIMPLE ANGIOMA OF THE ORBIT. E. CORNET, Ann. d'ocul. **171**:431, 1934.

Angioma of the orbit, known since first described by Abernethy, is subdivided into hemangioma, simple and cavernous, and lymphangioma. The latter is rare, there being only six cases recorded in the literature. Arlt was the first to employ alcohol for vascular tumors, while Maxxei used this method for angiomas of the lid.

As there does not appear to be any record of the application of alcohol to angioma of the orbit, a report of this case is published. Retrobulbar use of alcohol at from 80 to 90 F. was reported by Grüter and others. Klauber employed alcohol in 75 per cent concentration, two injections in the ciliary ganglion, in a glaucoma without any alteration of vision. Cornet used two retrobulbar injections of alcohol at 40 F. with an interval of twenty days between, but only after being assured, by the withdrawal of blood by means of a syringe, that he had entered the angioma.

The case is reported in detail, and there is also a bibliography.

McKEE, Montreal, Canada. [ARCH. OPHTH.]

THE HISTOGENESIS OF NEVI OF THE CONJUNCTIVA. K. OBERHOFF, Arch. f. Augenh. **108**:194, 1934.

Oberhoff believes that the nevi of the conjunctiva arise from an undifferentiated tissue which is morphologically associated with the walls of the smallest blood vessels. It is unnecessary to assume the intervention of tissue metaplasia in order to account for these tumors. ADLER, Philadelphia. [ARCH. OPHTH.]

A CASE OF NASAL ECTASIA OF THE FUNDUS WITH SUPERIOR AND INFERIOR CONUS. WALTHER LÖHLEIN, Klin. Monatsbl. f. Augenh. **93**:439 (Oct.) 1934.

A woman, aged 31, had myopic eyes with greatly elongated axes. Her right eye presented a myopia of 22 diopters with annular staphyloma, ectasia of the area of the macula and amblyopia since childhood. Her left eye had good vision until a few months prior to observation by Löhlein, when straight lines appeared wavy. The patient feared that a detachment of the retina had occurred. The fundus of the left eye presented a peculiar condition, which is minutely described, and the description is illustrated with a drawing and two photographs. The macular area showed only 2 diopters of myopia, but the nasal portion of the fundus was ectatic, with a myopia of 14 diopters. The occurrence of an ectasia at the nasal side of the fundus was due to superior and inferior conus and to the vessels entering the globe in an inverted direction, that is, in a medial direction. The descriptions of this phenomenon by E. Fuchs and von Szily Sr. and the embryologic research on it by von Szily Jr. are cited. Löhlein discusses the occurrence of upward and downward conus with inverted direction of the retinal vessels. Confusion of the condition with detachment of the retina is possible, and another oculist diagnosed retinal detachment later on, when vision had grown weaker. It had dropped from 5/7 to 5/50 of the normal when Löhlein had an opportunity to reexamine the patient a year after the first examination. This deterioration was due not to an increase of the ectasia but to an infection of the depigmented and

congenitally inferior, weak portion of the fundus. Sinusitis and chronic tonsillitis were considered as sources of the infection. Symptomatic treatment resulted in restitution of the vision to 5/7 of the normal. This case furnished proof (1) that the location of an ectasia of part of the fundus is less dependent on the location of the conus than on the direction in which the funnel of the vessels opens; (2) that congenital inferiority of the cover of the eye predisposes to progress of the destruction by stretching, as in the myopic ectasia in the temporal portion of the fundus; (3) that in congenitally abnormal eyes with a high degree of myopia the resistance of the tissues to incidental infectious diseases is diminished to some degree.

STOLL, Cincinnati. [ARCH. OPHTH.]

Diseases of the Ear, Nose and Throat

INFECTION OF THE PETROUS BONE. EINAR A. SUNDE, Arch. Otolaryng. **19**:436 (April) 1934.

Sunde cites the work of Profant, Eagleton, Voss, Kopetzky and Almour. The problem is to select patients who will recover without drainage of the petrous tip from those needing operative intervention.

Kopetzky advised hastening drainage in cases in which after the initial onset of pain in the eye, otorrhea and low grade sepsis there is a quiescent period, which he states is coincidental with the advance of infection into the epidural region about the tip. Sunde believes that this quiescent period might be also a stage of recovery and concludes:

1. While pain in the eye, fever and otorrhea persist without change, one should wait for developments.

2. If the symptoms increase and the patient becomes more irritable, with vomiting, increased headache, stiff neck or vertigo, one should explore the petrous tip, first seeking for fistula.

3. During the quiescent stage one should look for (*a*) increased otorrhea, indicating the unlocking of infection through a chain of cells by the same route through which the infection entered, and (*b*) decreased otorrhea, alone or coupled with no change, which indicates surgical intervention. The author prefers a modified Eagleton unlocking operation, if no fistula is present.

A case is reported.

GREENWOOD, Chicago.

FATAL COMPLICATIONS OF OTITIS MEDIA WITH PARTICULAR REFERENCE TO THE INTRACRANIAL LESIONS IN A SERIES OF TEN THOUSAND AUTOPSIES. CYRIL B. COURVILLE and J. M. NIELSEN, Arch. Otolaryng. **19**:451 (April) 1934.

Courville and Nielsen discuss autopsy observations in relation to the temporal bone with various subheadings such as infection of the meninges, abscess, thrombosis and encephalitis, and propose a plan for a postmortem study of cases under a number of headings. They have studied 10,000 autopsies at the Los Angeles General Hospital, which they have reported in a statistical study to be published in the *Acta oto-laryngologica*. The present article is concerned more particularly with the characteristics of the individual lesions, their interrelationship and their possible significance. The intermediate and transitional stages of intracranial lesions are frequently overlooked, especially mural thrombi. Occasionally the lesions are so varied that it is difficult to decide which is primary or to give an opinion as to their order of importance. A case is reported illustrating meningitis and otitis media associated with sinusitis, the sinusitis apparently being the actual source of the meningitis. Cases of this sort arising from ethmoid and sphenoid sinuses are discussed. Cases in which an abscess of the right parietal lobe was present, together with an infective thrombus of the right lateral sinus and a fistula from the middle ear, are discussed from the standpoint of the sequence of the lesions, and an effort is made to determine which lesion was primary. Otitis media is a frequent terminal lesion in infancy, either as a result of constitutional disease or

associated with bronchial pneumonia, enteritis, acute exanthems, etc. Otitis media was observed at 303 of 5,000 autopsies. The group is thoroughly analyzed from the standpoint of age and other lesions present and the complications present. The frequency of involvement of the petrous tip is, of course, carefully investigated, and three cases are reported illustrating petrositis and three illustrating thrombi or pus in the carotid artery. Intracranial complications of petrositis are discussed in detail. Extradural abscess usually indicates a fairly high degree of local resistance, which accounts for the fact that it is found so many times in operations with no other intracranial lesions. Statistics of the frequency of extradural abscess arising at different parts of the temporal bone are given.

Subdural abscesses are classified on an etiologic basis in the following manner:

"A. Extension by direct continuity through the bone and dura: 1. Direct spread, with no local reaction from the point of penetration through the bone and dura, usually over the tegmen tympani (3 cases). 2. With active local reaction and walling off of a small subdural abscess, usually located between the posterior surface of the petrous bone and the anterior margin of the cerebellum (4 cases). 3. Secondary breaking down of adhesions about a dural fistula, leading to a superficial cortical ulceration (1 case) or to an abscess in the temporal lobe (1 case).

"B. By retrograde extension along venous channels: 1. Regional, about the inferior cerebral veins or (rarely) about the superior cerebellar veins, afferent channels of the lateral sinus which was thrombosed (3 cases). 2. Distant, consequent to extension to distant points of the thrombotic process originating in the lateral sinus; (*a*) extension to the cavernous sinus (1 case) or to the superior longitudinal sinus (1 case); (*b*) extension by way of the anastomotic venous system (1 case).

"C. Rupture of an abscess of the brain into the subdural space. 1. Spontaneous rupture (0 cases). 2. Postoperative rupture into the subdural space following attempts at drainage (1 case—posterior fossa)."

Subdural abscesses are often overlooked, owing to the presence of other lesions. Seventeen cases are analyzed in relation to the lesion of the ear, and the association of sinusitis as a cause either in conjunction with otitis or as a separate entity is discussed. Charts and illustrations give the classification of subdural abscesses and show readily the various avenues of extension. Under "Thrombosis of the Intracranial Venous Channels" the various sites of the lesions are reported, with case histories illustrating intrasinus abscesses and illustrations showing various points in the body in which lesions might occur. A chart illustrating the various points in the brain, the site of complications of lateral sinus thrombosis, illustrates the text on this topic nicely. The pathologic lesions seen in otitic leptomeningitis and otitic encephalitis, nonsuppurative encephalitis and abscess of the brain are discussed in relation to the type of lesion and also the location. A protocol has been formulated for the study of postmortem material in cases with intracranial complications. Instructions are given for the exact procedure in examining the various parts. This thorough and interesting fifty page article cannot be adequately abstracted in a short space and should be read to be thoroughly appreciated.

HUNTER, Philadelphia. [ARCH. NEUROL & PSYCHIAT.]

TESTING THE HEARING OF THE PRESCHOOL CHILD. DOUGLAS MACFARLAN, Arch. Otolaryng. **19**:514 (April) 1934.

Macfarlan advises using a buzzing audiometer in testing the hearing of young children. The sound is transmitted over a telephone circuit in which a decibel meter has been placed. The child is previously trained to raise the hand when the sound (it must be loud) is heard and to lower it when the sound ceases. This is effected by having the instructor take the child's hand and go through the act until it is understood by the subject. Now the sound can be cut down, with a decibel meter used for accuracy. The child must not see the cut-off. Group testing is impracticable; only individual work is satisfactory.

In the test a phonograph record using common monosyllables in the vocabulary of a young child is placed on a phonographic audiometer. A decibel meter is

plugged into the audiometer on one side; the other side is led off to an ear-phone. The speech comes through at a single level of intensity until the meter is turned down. The child recites what he hears. As the meter reduces the intensity, he begins to miss words and to misinterpret. The reading on the meter at this point is referred to the reading for normal hearing.

Dr. Crowden has simplified this test by using a phonograph record of twelve common names, such as cat, dog and door. On a card placed in front of the child the names are illustrated. As the child hears the word he points to the proper picture. The intensity of the sound is reduced as with the present 4-A audiometer record. The level of intensity at which words are missed is the index of the loss of hearing.

GREENWOOD, Chicago.

SINUS DISEASE IN CHILDREN. REA ASHLEY, California & West. Med. **40**:156 (March) 1934.

Ashley considers the predisposing etiologic factors of sinus disease in children to be anatomic malformations, allergic tendencies, glandular dysfunction and poor general living conditions. The immediate etiologic factors are acute respiratory infections; the exanthems, especially pertussis and measles; contact with infected persons; swimming, and diving. The symptoms are manifold and include local and general manifestations. The diagnosis depends on the evaluation of the symptoms; the presence of two cardinal signs, namely, postcervical lymphadenitis and lateral pharyngitis, and the roentgen findings. Treatment consists of general and local measures. The latter are divided into medical treatment, with nasal packs of cotton saturated with hygroscopic colloidal and silver preparations, and conservative surgical treatment. The prognosis is good when treatment is undertaken early and carried out faithfully. Ashley emphasizes the necessity of close cooperation between the pediatrician, allergist and rhinologist in the solution of problems of handling complicated cases.

MARSHALL, San Francisco.

TONSILLECTOMY: BEFORE, DURING AND AFTER. R. F. GUYMER, Brit. J. Child. Dis. **31**:85 (April-June) 1934.

The term tonsillectomy as used here includes the removal of the adenoids in all cases in which this was found to be necessary. One hundred and eighty-two cases form the basis of this study. There is a discussion of the indications for tonsillectomy in infancy and later childhood. Guymer considers that dissection is the only satisfactory operation and that the guillotine should be relegated to the hospital museum. The signs and symptoms that head the list of those relieved by tonsillectomy in this small series of cases are enlarged cervical glands, mouth breathing, frequent sore throat and frequent colds in the head.

LANGMANN, New York.

ROENTGEN TREATMENT OF HYPERTROPHIED TONSILS AND OF RECURRING TONSILLITIS. A. GENTILI, Riv. di clin. pediat. **32**:769 (July) 1934.

Gentili reports thirty-five cases of children with enlarged tonsils with or without recurring tonsillitis who were treated by the roentgen rays. Records were made as to the condition of the tonsils one month, six months and one year after the treatment. The roentgen applications to the tonsils caused no subjective or objective disturbance in any case. In four cases good results, i. e., complete aplasia of the hypertrophied tonsils, were obtained; in five cases no effect was observed; in the other cases the shrinking in size was only slight and frequently only temporary. Twelve of the thirty-five children required tonsillectomy subsequently.

Histologic examination of the excised tonsils revealed regression of the lymphatic tissue and proliferation of connective tissue. Irradiation with the roentgen rays was more successful in diminishing the size of infected tonsils than of noninfected hypertrophied tonsils.

HIGGINS, Boston.

Diseases of the Skin

CUTANEOUS MANIFESTATIONS OF ARSENIC POISONING. SAMUEL AYRES JR. and NELSON PAUL ANDERSON, Arch. Dermat. & Syph. **30**:33 (July) 1934.

The authors point out the ubiquitous place of arsenic in modern life and emphasize that toxic reactions are not necessarily dependent on the amount of arsenic absorbed, for minute amounts are said to cause a severe reaction in a hypersensitive patient. The desirability of at least seven evidences in the support of arsenic as an etiologic factor in a given case is stressed: (1) a history of exposure, (2) the clinical appearance, (3) the presence of arsenic in the urine or hair, (4) the presence of arsenic in the tissue as revealed by microchemical stains, (5) a progressive diminution of arsenic in the urine together with clinical improvement under sodium thiosulphate therapy, (6) the recurrence of the symptoms on further contact with arsenic and (7) a positive patch test. A variety of cutaneous manifestations of arsenic poisoning were encountered in a series of cases.

DICK, Iowa City.

AUTOLYSATE THERAPY FOR VERRUCA VULGARIS. FRANK E. CORMIA, Arch. Dermat. & Syph. **30**:44 (July) 1934.

A wart autolysate was prepared after the methods suggested by Biberstein and Soule. Twelve patients were treated, each receiving at least ten injections of autolysate. In only two cases was cure effected, and here the specific immunologic action was questionable. The immunologic treatment of warts was generally ineffective in this series.

DICK, Iowa City.

DERMATITIS EXFOLIATIVA NEONATORUM. FRANK C. NEFF, Arch. Pediat. **51**:465 (July) 1934.

A case of dermatitis exfoliativa neonatorum with recovery is presented. Neff accepts the statement in the recent edition of Holt and McIntosh that this condition should be regarded as a "symptom complex" rather than as a disease. It is thought that the symptom complex may be a complication of more than one primary disease, particularly of impetigo neonatorum and measles.

WADDELL JR., University, Va.

PIGMENTED NEVI. EUGENE F. TRAUB, Arch. Pediat. **51**:516 (Aug.) 1934.

In a previous article appearing in the *Archives of Pediatrics* Traub discussed the classification of nevi and the treatment of vascular nevi. The present article is concerned with the pigmented nevi and moles. The various theories of histogenesis are discussed and outlines of treatment suggested.

WADDELL JR., University, Va.

VON RECKLINGHAUSEN'S DISEASE. MARK S. REUBEN, Arch. Pediat. **51**:522 (Aug.) 1934.

A case of von Recklinghausen's disease occurring in an infant is presented, together with a review of the literature on this subject.

WADDELL JR., University, Va.

SENSITIVITY TO FUNGI IN INFANTILE "ECZEMA." L. W. HILL, J. A. M. A. **103**:331 (Aug. 4) 1934.

Trichophyton infection apparently is not of much importance in the eczemas of infants and children. Intracutaneous tests for Monilia albicans were positive in 15 per cent of eczematous infants and young children and in 8 per cent of a series

of normal controls. It seems likely that monilia infection is of importance in infantile eczema and that the monilia test is worth while in all cases in which there are scaly lesions on the inner side of the thighs, around the anus and on the fingers, with involvement of the nails, or patchy flat lesions on the body. While the cases here reported have not proved to be cases of monilia infection, the evidence indicates strongly that they may be.

BONAR, Salt Lake City.

SKIN REACTIONS IN INFANTS: SUSCEPTIBILITY OF THE SKIN OF THE NEWBORN TO PASSIVE ATOPIC SENSITIZATION; COMPARISON WITH REACTIONS TO HISTAMINE. T. NELSON CAREY and LESLIE N. GAY, J. Allergy **5**:488 (July) 1934.

The study was undertaken in order to determine the age at which children might be expected to react positively to intradermal testing with atopen. Passive transfer technic was used.

The authors' conclusions are: 1. New-born infants can be passively sensitized to ragweed by the Prausnitz-Küstner method. 2. When higher concentrations of test solutions are used the reactions resemble those observed in adults. 3. Marked variations are noted in the dose of atopen required to produce reactions of the same intensity in the skin of different infants when the same serum is used for sensitization. 4. The smaller and variable reactions noted in the skin of the newborn, when tested in this manner, correspond closely to the small and variable reactions following the intradermal injection of histamine.

HOYER, Cincinnati.

TREATMENT OF PSORIASIS WITH A GOLD SALT (GOLD SODIUM THIOSULPHATE). ALBERIC MARIN and F. L. BOULAIS, Union méd. du Canada **63**:634 (July) 1934.

Sixteen patients with psoriasis were treated with gold sodium thiosulphate, each receiving from seven to eighteen weekly intravenous injections. Four patients were definitely helped, and three others showed slight improvement. Three months later the lesions had all recurred. One patient seemed to be made worse by the treatment. Eight of the patients had reactions consisting of nausea or erythema. Marin and Boulais conclude that the treatment is not without its dangers and that it does not possess the desired efficacy against psoriasis.

DAFFINEE, Boston.

THE TREATMENT OF LUPUS VULGARIS. SVEND LOMHOLT, Brit. M. J. **2**:291 (Aug. 18) 1934.

This article is a general discussion of the features and characteristics of lupus vulgaris, with a history of the treatment which has been employed in the past. A description of the treatment used in the Finsen laboratories follows, with special reference to a modification of the earlier treatment with the quartz mercury vapor lamp.

ROYSTER, University, Va.

CALCINOSIS. W. D. W. BROOKS, Quart. J. Med. **3**:293 (July) 1934.

The literature concerning calcinosis is reviewed. Brooks then presents the results of his own experimental study concerning the calcium and phosphorus balance in a case of calcinosis in a girl of 15 years and also in a case of sclerodermia in a woman aged 41 years. In the girl, pathologically high levels of serum calcium, plasma inorganic phosphate and plasma phosphatase were maintained over a long period, whereas these values were normal in the case of sclerodermia. The calcium metabolism in the case of calcinosis was restored to approximate balance by the administration of disodium hydrogen phosphate. The author suggests that in calcinosis a local tissue change, not yet clearly understood, results in localized damage to fibrous tissue and that when calcification occurs in these areas an abnor-

mality of calcium and phosphorus metabolism may also occur. Brooks thinks that the type of lesion in sclerodermia does not necessarily produce abnormal changes of the calcium and phosphorus metabolism. BRADFORD, Rochester, N. Y.

ACRODYNIA: TREATMENT BY PHYSICAL THERAPY. J. LABORDERIE, Arch. d'électric. méd. **42**:82 (Feb.) 1934.

In a 4 year old child who had an attack of acrodynia two weeks before, a first series of twelve exposures to the ultraviolet rays produced improvement in the general condition, in sleep and even in gait, but the psychic and sensory disturbances diminished perceptibly only during a second series administered after a rest of ten days. Another patient, 26 months old, who was affected three weeks before, was treated according to Bordier's regimen for infantile paralysis by means of spinal radiotherapy and diathermy, with the addition of irradiation with the ultraviolet rays. From the first treatment improvement was seen, and in three weeks the physical and psychical recovery was complete. VINTON, Brooklyn.

INFANTILE ACRODYNIA: REPORT OF TWO CASES. E. PICHON and H. CAMBESSÉDÈS, Arch. de méd. d. enf. **37**:404 (July) 1934.

Two cases of acrodynia are reported in detail. The first is that of a girl of 16 months. The diagnosis was in doubt, and the patient was treated tentatively for muscular hypotonia and myasthenia until a visitor to the children's wards from Australia detected the characteristic syndrome. The same consultant also suggested the use of potato in the diet, with the skin of the potato included so as to permit the patient to profit by an antiacrodynic substance alleged to exist directly underneath. Various remedies had been employed for several weeks, including the subcutaneous injection of sodium cacodylate, of acetylcholine and of strychnine, together with exposure to ultraviolet rays, without the slightest effect. From the first day on the potato regimen the patient began to improve rapidly and was discharged recovered within three weeks. The authors wisely call attention to the fact that in the normal evolution of acrodynia the time had arrived for spontaneous cure. They follow this history with that of another patient, a boy of 20 months, who was treated in his home for scarlet fever in June 1933. Recovery was slow; the patient's appetite was lost; he cried a great deal and refused to walk or even sit up in bed. He entered the hospital about ten weeks after the onset with marked palmoplantar desquamation; two days later a morbilliform eruption on the trunk was noted. The case was considered one of measles complicating the course of prolonged convalescence from scarlet fever, until careful examination showed complete absence of catarrhal symptoms and Koplik's spots. Swelling of the hands and feet with cold perspiration was observed during the following weeks, together with pronounced psychic disturbances, and the diagnosis was changed to acrodynia. In spite of vigorous treatment, including the use of potato, the child gradually grew worse and died in November of bronchopneumonia. AMESSE, Denver.

THE SO-CALLED MONGOLIAN SPOTS IN THE NEW-BORN OF THE NEGRO RACE. M. METZGER and J. CLARIN, Bull. Soc. d'obst. et de gynéc. **23**:442 (July) 1934.

The authors briefly discuss the incidence of Mongolian spots in Asiatic races and mention the conflicting opinions and few observations regarding their presence in the black races. They report their observations on a series of fifty-three native infants of the black race observed on the Ivory Coast of Africa. Thirty-three, or 62 per cent, of these infants had Mongolian spots in the typical forms and locations. Between the ages of 6 months and 1 year the bluish color of the spots so blends with the normal dark color of the skin that they can no longer be distinguished. The opinion of the authors is that Mongolian spots cannot be considered as a peculiar property of the Mongolian race.

GLASER, Rochester, N. Y.

ERYTHEMA NODOSA AND PHLYCTENULAR CONJUNCTIVITIS. NOBÉCOURT and DUCAS, Presse méd. **42**:1241 (Aug. 4) 1934.

The finding of erythema nodosa and phlyctenular conjunctivitis in the same subject is rare. As both lesions usually have a tuberculous origin the report becomes of greater interest.

An 11 year old girl was seized with fever, headache, fatigue and anorexia. In four days an eruption characterized by violet and red papules appeared on the lower extremities and was confined there throughout the attack. The nodules were from 2 to 3 cm. in diameter and appeared in groups of seven or eight. They were slightly mobile, presented a prominent center and an indecisive periphery and appeared set in the surface of the skin. Certain of the lesions were new, appearing as ecchymotic spots; others were old and seemed about to disappear. Physical examination and the roentgenogram of the lungs showed definite evidence of pathologic changes at the hilus. The father had died of tuberculosis. One month after the child entered the hospital, a lesion appeared on the conjunctiva of the left inferior lid. The ophthalmologic consultant, not knowing of the patient's general condition, pronounced the palpebral condition phlyctenular conjunctivitis. A tuberculin test was positive. Guinea-pigs inoculated with the patient's blood showed tubercle bacilli in the inguinal glands at autopsy. The authors are inclined to agree with the statement of Fornara that such lesions become apparent when the patient is in a hyperallergic state. A chart, roentgenogram and bibliography are given.

MAYER, Chicago. [ARCH. OPHTH.]

DIET IN THE ECZEMA OF INFANCY. JULIAN T. RUBIO and F. RODRIGO PALOMARES, Pediatría españ. **23**:240 (July) 1934.

The authors mention various feeding regimens which have gained much favor and are widely used. In general, it seems advisable to keep the intake of milk and milk products low. Some regard drastic reduction in quantity and modification, especially in the fat content, as adequate measures; others discard the use of milk entirely and advise the use of milk-free substitutes, for example, soy-bean milk. There is also general agreement that the salt content of the diet must always be low.

SCHLUTZ, Chicago.

DESENSITIZING EXPERIMENTS IN ECZEMA. MARTIN KREBS, Monatschr. f. Kinderh. **60**:445, 1934.

Krebs tried the desensitizing technic of Lambert-Aucel-Bouion on twenty-seven children. This consists of giving a minimal amount of the symptom-eliciting food from three quarters of an hour to one hour before the meal, with the purpose of producing the antianaphylaxis state of Besredka. If the child is on the breast one drop of breast milk is given, or if the child is sleeping a pipet is used to place a drop in the carefully opened mouth. For the child on a solid diet a pea-sized morsel in a teaspoonful of water is used. The preliminary feeding must contain all the suspected foods. Krebs claims that fourteen of his twenty-seven patients were cured and nine improved. The treatment must last at least fourteen days and sometimes three months.

GERSTLEY, Chicago.

THE ROENTGEN RAY TREATMENT OF SKIN DISEASES. F. BERING, München. med. Wchnschr. **81**:1119 (July 27) 1934.

Bering discusses the treatment of numerous diseases of the skin with the roentgen rays. The more that is learned about the action of the roentgen rays the more limited becomes their application. He mentions some diseases of the skin of interest to the pediatrician. For favus an epilating dose is used; this is repeated in three or four months if there is a recurrence. Other conditions successfully treated are actinomycosis of the skin and lymph nodes; furuncle, particularly of the upper lip; erythema induratum of Bazin; pernio; papulonecrotic tuberculid, and

scrofuloderm. In lupus vulgaris better results are obtained with other treatment. The roentgen rays should not be used for the eczema of children. In fact, Bering states that children should not be treated with the roentgen rays for diseases of the skin. The dangers of exposing children to even the smallest doses has not been realized sufficiently.

BRAHDY, Mount Vernon, N. Y.

THE OUTBREAK OF ERYTHEMA NODOSUM IN A SCHOOL. W. GOBEL, Ztschr. f. Kinderh. **55**:30 (May) 1933.

Gobel describes an outbreak of erythema nodosum in school children which was traced to a teacher suffering from open tuberculosis. The erythema nodosum was preceded by an angina, and the symptoms were: malaise, fever, vomiting, diarrhea, cervical adenitis, stiffness of the neck and bronchitis. The disease was most common in spring and was more frequent in girls than in boys. The tuberculin reaction was positive in seventy-three of the one hundred and seventeen children, or in 62.4 per cent. It was positive in twenty-eight of the fifty-three boys, or 52.8 per cent, and in forty-five of the sixty-four girls, or 70.3 per cent.

LEVINSON, Chicago.

CHANGES IN THE BLOOD AND THE FUNCTIONS OF THE SKIN IN ECZEMA. S. FEDOSEWICZ, Przegl. dermat. **29**:270 (June) 1934.

In a study on thirty cases of eczema Fedosewicz made the following observations regarding the changes of the blood picture and the reactions of the skin to different substances: In nearly all the cases there was a shift of the leukocyte formula to the left, the index varying from 0.09 to 0.33. Eosinophilia and lymphocytosis predominated; monocytosis was more rarely observed, and in one case monocytopenia was present. The percentage of hemoglobin was frequently low. Fedosewicz carried out on the same patients intradermal tests with physiologic solution of sodium chloride, sterilized milk, staphylococcus and streptococcus vaccine, tuberculin solution and two proprietary preparations. He read the reactions half an hour, twenty-four and forty-eight hours after the injection. With the exception of eleven negative reactions to physiologic solution of sodium chloride and two negative reactions to sterilized milk all the reactions were positive, the intensity of the reaction depending on the agent used. In comparing the reactions produced by the staphylococcus and streptococcus vaccine it was found that in the majority of cases the former produced a much stronger reaction than the latter. No proportionate relation was noted between the intensity of the cutaneous reaction and the number of eosinophils or monocytes in the blood. The cutaneous reactions which appeared late were much stronger than those which appeared early. In two cases in which the early intradermal reaction was the stronger there was noted a weak humoral manifestation of the allergic process; the leukopenia and lowering of the blood pressure were only of slight degree.

BLOOM, New York. [ARCH. DERMAT. & SYPH.]

INFLUENCE OF THE NERVOUS SYSTEM ON THE REACTIVITY OF THE SKIN (CLINIC OF NERVOUS AND SKIN-VENEREAL DISEASES). V. A. TUMSKAYA and D. A. TRUTNEV, Vrach. delo **17**:207, 1934.

The investigation of the clinic brought out that the application of the method of percutaneous reactions in cases of organic disturbances of the nervous system may yield a number of results valuable in the solution of questions pertaining to dermatology and neuropathology. Investigations of dermatitis in organic disturbances of the nervous system definitely showed the influence of the nervous system on the allergic reaction of the skin.

It is recommended that further investigations of the mechanism of the influence of the nervous system on skin reactions of the allergic type be carried on.

YAMPOLSKY, Atlanta, Ga.

LEUKOCYTIC PHAGOCYTOSIS IN ECZEMA AND DERMATITIS. ECZEMATOUS CHANGES IN THE SKIN AND LEUKOCYTIC PHAGOCYTOSIS. THE KOTTMANN REACTION IN SOME TYPES OF DERMATOSES. TOHL OZAKI, Jap. J. Dermat. & Urol. **36**:121, 143 and 160 (Aug.) 1934.

In a series of articles Ozaki reports his observations on phagocytosis in clinical and in experimental (croton oil) dermatitis in rabbits and on the Kottmann reaction.

In both the artificially induced and the clinical dermatoses there was, during the acute stages, the same striking diminution in the phagocytic power of the leukocytes; in the subacute and convalescent periods there was an irregular return to normal. In the experimentally induced inflammatory reactions it could be demonstrated that the decrease in the number of particles of pigment (india ink preparation) taken up by the leukocytes was numerically in inverse ratio to the increase in the leukocyte count.

The Kottmann reaction was found to be accelerated, especially in early syphilis, in acne vulgaris and in some of the eczemas; it was retarded in keratodermia palmaris progressiva. Ozaki admits that this might suggest, respectively, overactivity or underactivity of the thyroid gland in these conditions, but he does not believe that the Kottmann reaction can be employed to measure directly the activity of the thyroid gland.

[ARCH. DERMAT. & SYPH.]

ERYTHEMA NODOSUM. J. C. SCHIPPERS, Maandschr. v. kindergeneesk. **3**:371 (June) 1934.

In this survey the author concludes that erythema nodosum is often the manifestation of a fresh tuberculous infection and that the patient is often dangerous to surrounding persons. Children with this disease should be closely observed and should be isolated during the period of contagion. Search for the origin of the infection is necessary.

VAN CREVELD, Amsterdam, The Netherlands.

ECZEMA AND HYDROGEN ION CONCENTRATION OF THE BLOOD PLASMA. K. EDEL, Nederl. tijdschr. v. geneesk. **78**:3673 (Aug. 11) 1934.

The author determined the hydrogen ion concentration of the blood plasma of forty-seven patients with different forms of eczema. The values obtained differed from the normal ones in twenty-four cases (under 7.3 or above 7.4). By the administration of acids or alkalis in some patients restoration to the normal p_H was obtained; in other patients no change in the p_H was brought about. Edel concludes from the results obtained that deviations from the normal values p_H do not have any influence on the seriousness of the disease, nor has restoration of the normal p_H any influence on the time necessary for the healing of the eruption.

VAN CREVELD, Amsterdam, The Netherlands.

Surgery and Orthopedics

PROCEDURES IN CLEFT PALATE SURGERY. ROBERT H. IVY and LAWRENCE CURTIS, Ann. Surg. **100**:502 (Sept.) 1934.

Ivy and Curtis discuss the works of Victor Veau and offer his classification of cleft palate with the choice of time for operation as follows: (1) cleft limited to the soft palate, from 2½ to 4 years of age; (2) median cleft of the hard and soft palate, from 2½ to 4 years of age; (3) complete unilateral cleft, from 3 weeks to 3 months of age; (4) bilateral cleft, from 3 weeks to 3 months of age. The operation of Veau is described, with illustrations. A summary of the cases of fifty-three patients who were operated on is given.

BANTIN, Omaha.

PROPHYLACTIC MEDIASTINOTOMY FOR PERFORATING ESOPHAGEAL FOREIGN BODIES; REPORT OF THREE UNUSUAL CASES. FRANCIS L. LEDERER and LOUIS ZOLO FISHMAN, Arch. Otolaryng. **19**:426 (April) 1934.

Lederer and Fishman state that esophageal foreign bodies, when pointed and embedded against the plane of removal, are not removed without laceration. They emphasize the uncertainty as to whether or not a prophylactic mediastinotomy is advisable following perforation and give the view of the Vienna school that this operation must always be carried out below the known site of perforation, which is in either the first postcricoid or the second natural (aortic) narrowing. They criticize Clerf for his statement that the development of mediastinitis following esophagoscopy indicates delay and that if it develops in the absence of instrumentation esophagoscopy might be indicated by stating that Clerf does not state whether his rationale is based on the presence of a foreign body or what he would do if it had already been removed and makes no definite note of descending mediastinitis. They note that Carmody's statement that practically all patients on whom the external operation is performed die is too dogmatic. They refer to Orton's stand of nonintervention until walling off is effected and placing the esophagus at rest, followed by operation by a thoracic surgeon, and state that the vital question of intervention by the laryngologist with mediastinotomy is omitted. They agree that conservatism is the best method. The article contains reports of three cases of perforation or supposed perforation with recovery without any surgical intervention. It is concluded that the greatest number of patients do not survive periesophageal infections following perforation by foreign bodies and that many prognoses may be improved by prophylactic mediastinotomy.

GREENWOOD, Chicago.

PAINFUL HEELS AMONG CHILDREN (APOPHYSITIS). H. W. MEYERDING and W. G STUCK, J. A. M. A. **102**:1658 (May 19) 1934.

The epiphyses of the heels of healthy children are often injured. Mild symptoms normally divert suspicion from the heels, and roentgenograms are rarely taken. Undue strain on the calcaneal epiphysis during the period of greatest growth engenders an appreciable amount of epiphyseal change that is never discovered. An etiologic factor is the common practice of engaging in vigorous games in heelless athletic shoes. Roentgenologically, in the lateral view the epiphysis of the heel is flabby, moth-eaten, somewhat flattened or partially fragmented, and there is usually considerable irregularity of the adjacent posterior surface of the calcaneum with cloudiness and irregularity of the epiphyseal line. Treatment consists of local heat and massage and elevation of the heels with heel pads. The authors believe that this condition is commonly unrecognized.

BONAR, Salt Lake City.

HERNIA INTO THE UMBILICAL CORD CONTAINING THE ENTIRE LIVER AND GALLBLADDER. W. A. NIEBUCHR, C. A. DRESCH and F. W. LOGAN, J. A. M. A. **103**:16 (July 7) 1934.

Usually only loops of the intestine are found in hernia into the umbilical cord, but in the case reported the liver and gallbladder were the contents. A successful operation was performed twenty-one hours after birth.

BONAR, Salt Lake City.

ACUTE OSTEOMYELITIS: A CLINICAL AND EXPERIMENTAL STUDY. KEENE O. HALDEMAN, Surg., Gynec. & Obst. **59**:25 (July) 1934.

Following the production of experimental osteomyelitis in thirty-three rabbits by introducing cultures of Staphylococcus aureus into the tibia through a drill hole near the upper end of the bone, the pathologic observations were recorded:

"1. The blood vessels become engorged and the bacteria are walled off by fibrin, pus cells, macrophages, and fatty tissue forming definite zones in the order named.

from within outward. 2. Newly formed bone (involucrum) which appears after 1 week, comprises the outer shell of the defensive wall and also replaces necrotic bone. 3. The separation of dead bone (sequestrum) from the living cortex takes place after 2 or 3 weeks by means of thrombosis of the vessels in the haversian canals which in turn become enlarged and invaded by osteoclastic cells. 4. The bone marrow is replaced by fibrous tissue containing many fat cells. 5. In the chronic stage the contour of the bone is restored by involucrum, and the sequestra float unattached in an abscess cavity."

Six clinical cases are reviewed in detail. In all but one there was a history of infection of the skin or sore throat from one week to one month before the onset of the symptoms of osteomyelitis. The process usually begins in the shaft close to an epiphyseal line and spreads through the haversian canals outward to form a subperiosteal abscess which eventually lifts up periosteum from a large area. As early as five days after the onset of symptoms the roentgen rays may reveal a focus of rarefaction at the site of the beginning process in the bone. Blood cultures made during the acute stage are positive for Staph. aureus in a large proportion of cases, and infection of the blood stream may be discovered before that in the bone. Within a few days after drainage of the diseased bone cavity blood cultures usually become negative. Operation is indicated as soon as the diagnosis of probable osteomyelitis is made. Orr's method of securing drainage through a window in the cortex, completely exposing the infected portion of the medullary cavity, gives good results. A petrolatum pack is employed to keep the wound open, and immobilization to insure rest and prevent contamination is maintained by a plaster cast. Other methods of frequent dressing, including the use of irrigations with surgical solution of chlorinated soda, are also of value. The removal of sequestrums should be postponed usually for from two to three months after the primary operation in order to permit formation of sufficient involucrum to maintain the continuity of the bone.

GRAVES, New York.

ADOLESCENT KYPHOSIS. J. M. EDELSTEIN, Brit. J. Surg. **22**:119 (July) 1934.

In this article Edelstein describes a condition known as osteochondritis deformans juvenilis dorsi, which was first described fully by Scheuermann of Copenhagen and often is referred to as Scheuermann's disease. This type of kyphosis has to be distinguished from that due to tuberculosis, rickets or relaxed round back of school children.

Clinically, it occurs more frequently in boys between the ages of 12 and 17 years. The first symptom is usually curvature of the dorsal region of the spine. On examination of the back as a whole there is very little rigidity or no rigidity on active movement, but the region of the kyphosis is completely fixed and can be neither actively nor passively corrected. The kyphosis is not sharp but gradually rounded and smooth, the most prominent site being below the seventh to the tenth dorsal vertebra. The thoracic cage acquires a domelike character. Roentgenographic changes are best seen in a lateral view of the spine. There is rarefaction of the epiphyseal plates. Their outline is irregular, and the edges are frayed. The adjacent vertebral bodies show indistinctness of outline above and below. As the process is more marked anteriorly than posteriorly the anterior surfaces of the vertebrae become shorter than the posterior, resulting in deformity.

This process may proceed rapidly, but as a rule it is slow, covering many years. This process of destruction usually subsides at the time that fusion of the epiphyses occurs, which is the end of the period of growth. Although the bodies of the vertebrae become normal, the disks remain wedge-shaped.

Eight cases are cited in which this condition was found. At present its etiology is obscure, though many theories have been advanced, such as nutritional defect, biochemical disturbances, derangement of epiphyseal development, and Schmorl's theory of nuclear hernia.

Treatment consists of complete recumbency in order to reduce weight-bearing on the affected column. Later, a plaster jacket and leather support are used.

SUMMERFELDT, Toronto, Canada.

Perforative Appendicitis Complicating Acute Nephritis in an Infant. J. B. Marinan, Brit. M. J. **1**:1166 (June 30) 1934.

A 5 month old girl died of acute nephritis. At autopsy there was a perforated appendix with free pus in the pelvis.

Royster, University, Va.

Preservation of the Umbilicus in the Radical Cure of Umbilical Hernias in Children. R. Wood Powell, Brit. M. J. **2**:353 (Aug. 25) 1934.

Attention is called to the fact that when umbilical hernias need a radical operation a scar is often left with no semblance of a navel. This causes embarrassment to the patient and sometimes produces a morose reaction. Powell thinks that removal of the umbilicus in this operation is entirely unnecessary and believes that the operation of Victor Bonney, with the use of a long abdominal incision through the umbilicus in the midline and reforming of the umbilicus at the conclusion of the operation, is wise.

Royster, University, Va.

Unusual Form of Congenital Coxa Vara with Platyspondylisis. N. Josserand and Pouzet, Lyon chir. **31**:469 (July-Aug.) 1934.

A girl of 10 exhibited disproportion between the trunk and limbs. She was 93 cm. tall, with arms 43 cm. long and legs 51 cm. long. Her sitting height, measured from the occiput by way of the vertebral spines, was only 38 cm. The lumbar depression was very marked, being emphasized by flexion of the thighs, correction of which did not affect the depression. There was a slight middorsal scoliosis to the right, but nevertheless the thorax was shaped like the keel of a boat, with a forward projection of the abbreviated sternum. Her gait was unsteady, with balancing of the body. The Trendelenburg sign was present. On roentgenograms of the thighs slight epiphyseal ossification was seen: half the cartilaginous head was united to the diaphysis, but no interstitial cartilage and no neck were seen. Stereoscopy showed a large acetabulum with bony concretions of the head in its center, while the diaphysis was directed backward and the great trochanter lay in the iliac fossa without contact with bone. The pubis was not ossified, and the iliac alae were very broad, the pelvis being flattened transversely. Platyspondylisis of the vertebral column was general, with posterior rachischisis of the cervical vertebrae and anomalies of the fourth and fifth dorsal vertebrae.

Vinton, Brooklyn.

Paralysis of the Lower Extremities in a Case of Tuberculosis of the Spine. B. Savino, Prat. pediat. **12**:317 (July) 1934.

Savino describes a child in whom kyphosis, then an inguinal fistula and after two months paralysis of the lower extremities developed. The roentgen rays showed complete destruction of the fourth and fifth lumbar vertebral bodies. The particular interest in this case lies in the fact that the child was only 3 years old.

Dooley, New York.

Osteomyelitis and Purulent Perinephritis in the Nursling. Saul I. Bettinotti and Genaro García Oliver, Arch. argent. de pediat. **5**:325 (June) 1934.

The authors encountered this condition in an infant aged 3 months. The left shoulder was involved. This was treated by open drainage. A tumor mass discovered in the right flank proved to be a perinephritic abscess. Culture from the latter lesion showed staphylococci and a gram-positive diplococcus.

Schlutz, Chicago.

TREATMENT OF EMPYEMA IN THE INFANT. JOSÉ S. CASTRO, Rev. chilena de pediat. **5**:331 (June) 1934.

The condition is extremely grave in the young infant. The mortality runs as high as 32 per cent. Pneumonic processes are primarily the cause. Pneumococci are found in 70 per cent of the cases, staphylococci in 7 per cent, streptococci in 5 per cent and colon bacilli in 1.75 per cent. Only a small proportion of patients are cured by repeated thoracic puncture and aspiration. The author prefers puncture followed by thoracotomy and semiclosed drainage with the tube of Delbet. If this does not relieve the condition, rib resection is indicated.

SCHLUTZ, Chicago.

FRACTURE OF THE ELBOW IN CHILDREN: SEPARATION AND DISLOCATION OF THE PROXIMAL EPIPHYSES OF THE RADIUS. R. R. VON OPPOLZER, Deutsche Ztschr. f. Chir. **243**:427 (June 30) 1934.

Fracture and dislocation of the proximal epiphysis of the radius is a typical lesion in injuries to the elbow in children between 4 and 15 years of age. This is most frequently caused by indirect violence, with displacement of the fragment laterally and anteriorly. A "bloodless" operation is described for the treatment of this condition, the principle of which is as follows: Under anesthesia the forearm is extended and supinated over the thigh of the operator as a fulcrum. This causes a widening of the cleft of the joint between the humerus and the radius. The thumb of the operator now exerts pressure from the side on the dislocated fragment, while at the same time the lower arm is slowly pronated and flexed at the elbow. While this maneuver is being executed the dislocated fragment is easily forced into place. The pressure of the thumb is not exerted anteriorly to avoid injury to the radial nerve. The dislocation is not likely to recur if extreme pronation and supination are avoided. The arm should be held in slight pronation with the elbow flexed by means of a dorsal splint extending to the wrist. Healing requires from two to three weeks.

GLASER, Rochester, N. Y.

RAMMSTEDT OPERATION FOR PYLORIC STENOSIS IN INFANTS. H. VON HABERER, München. med. Wchnschr. **81**:903 (June 15) 1934.

Haberer reviews the results that he obtained in one hundred and two Rammstedt operations for pylorospasm. If the latest refinements in technic are used the results are excellent and the operative mortality low. In cases in which the operative mortality is high it is usually because the operation is performed too late, so that in spite of a successful operation the infant cannot recover. However, not every infant with pylorospasm requires operation. Cooperation between the pediatrician and the surgeon will improve the results of both the conservative and the operative treatment. So long as there is no unanimity of opinion as to the indications for operation statistics of the operative results must be evaluated critically.

BRAHDY, Mount Vernon, N. Y.

HABITUAL SPINAL CURVATURES AND THEIR TREATMENT. GAUGELE, München. med. Wchnschr. **81**:1344 (Aug. 31) 1934.

Gaugele calls attention to the frequency of poor posture and emphasizes the harmful permanent changes in body mechanics which may follow if it is not corrected. Numerous exercises are described for the treatment of the various postural defects.

BRAHDY, Mount Vernon, N. Y.

PRIMARY PSOASITIS IN THE CHILD. POPESCO-SÉVERIN and G. PODENANO, Spitalul **54**:269 (June) 1934.

The authors, after reviewing an article by Ingelrans and Minne, decided to look up the cases of this condition in their clinic at Bucharest. They found 0.4

per cent of primary psoasitis of the kind reported by Ingelrans. In the majority of instances the disease was due to superficial infections of the lower extremities. In three cases only it was due to direct traumatism in the lumbar region. In two cases, the treatment was medical and radiotherapeutic; in the remaining cases it was surgical. Incision was made below the crural arch nine times and in the lumbar region one time. Three patients died. Necropsy showed that the collection of pus was situated either above or below the psoas muscle at the iliac attachment. Microscopic examination revealed degenerative lesions of the muscle fibers, increase of connective tissue and infiltration by leukocytes. It seemed to the authors that the psoasitis was due to an infection of lymphatic origin, usually secondary to inflammation of the external iliac glands or those of Brault.

AUTHORS' SUMMARY.

TORSION OF THE TESTIS. R. J. HARRENSTEIN, Nederl. tijdschr. v. geneesk. **78**:2842 (June 23) 1934.

Two patients, 6 months and 16 years old, respectively, were operated on for torsion of the testis. A review is given of the principal data in the literature on this little known clinical picture. A more widespread knowledge of this disease is desirable because a distinct and early recognition of the condition is essential in deciding on an operation early enough to save the function of the organ.

VAN CREVELD, Amsterdam, The Netherlands.

Miscellaneous

LEAD POISONING IN CHILDREN. H. B. CUSHING, A. E. CHILDE, L. J. RHEA, I. M. RABINOWITCH, H. S. MITCHELL and S. G. ROSS, Internat. Clin. **1**:189 (March) 1934.

I. *Introductory Remarks* (H. B. Cushing).—Observations were made on a series of seventeen cases of lead poisoning seen in one year, two of them fatal. The cerebral symptoms were more frequent than lead line, colic and wristdrop. Usually there was a history of chewing paint from cribs, toys or pencils. Rapidly drying enamels contain no lead. The cheaper beds, especially those painted at home, and the cheaper toys, especially those painted yellow or green, contain the most lead. The paint used on cheap yellow pencils frequently contains lead.

II. *Roentgen Observations* (A. E. Childe).—Normal growing bones show a narrow white line at their growing ends. In lead poisoning these lines are denser and wider. Their width is dependent on the amount of growth during the ingestion of lead. Changes are seen at the ends of all long growing bones.

III. *Biochemical Aspects* (I. M. Rabinowitch).—The toxicity of lead is related to the solubility of its compounds in human serum. The higher incidence of encephalopathies is explained by the fact that metallic lead is ten times, and lead oxide twenty-five times, more soluble than lead sulphate. Lead chromate is changed by chemical action in the body to a very soluble compound. Storage and mobilization of lead within the body are largely dependent on its solubility.

IV. *Pathology* (L. J. Rhea).—In the more acute cases the central nervous system shows meningo-encephalitis. Postmortem observations in two cases showed a complete change in the character of the epiphyseal lines in the bones. "Instead of spongy delicate tissue which blended with the adjacent parts there were compact, quite dense, longitudinal trabeculae, in which numerous cartilage cells were present. Between these trabeculae there was deposited connective tissue of varying density, which had almost completely replaced the normal inter trabecular tissues." The brain showed edema of the meninges and dilatation of the blood vessels of the brain substance, with areas of perivascular lymphocytic infiltration, microscopic hemorrhages, hyperplasia of vascular epithelium and areas of degeneration.

V. *Clinical Study* (H. S. Mitchell).—The symptoms in twelve cases are detailed. These were, in the order of their frequency: pallor, convulsions, drowsiness,

meningeal irritation, vomiting, constipation, paralysis, headache, muscular incoordination, colic and loss of weight.

VI. *Treatment* (S. G. Ross).—When symptoms are present it is advisable to remove lead from the circulation by promoting storage in bone, where it is innocuous. This is accomplished by giving 1 quart (946.36 cc.) of milk daily plus from 2 to 4 Gm. of a soluble calcium salt, such as the gluconate. Calcium chloride should not be given, as this causes acidosis and sets free lead in the circulation. Magnesium sulphate in a dose of 5 cc. of a 25 per cent solution is recommended to relieve convulsions due to cerebral edema.

After all the acute symptoms have subsided, "deleading" should be attempted in the hospital. A low calcium diet, such as one of bread, potatoes, rice, tomatoes, bananas, apples and corn meal, is given. An acid-producing substance like ammonium chloride in divided doses of from 3 to 5 Gm. daily is given. This treatment should be given for one week, followed by rest. With the appearance of any toxic symptoms the deleading treatment should be stopped and storage of lead promoted. Two or three courses of deleading are usually given.

MILLER, South Bend, Ind.

SUPRARENAL AND THYROID GLAND THERAPY IN THE FUNCTIONAL DISORDERS OF INFANCY. ORVILLE BARBOUR, M. Rec. **140**:188 (Aug. 15) 1934.

Vomiting, colic, coughing, attacks of dyspnea and cyanosis, nervous irritability and various cutaneous rashes for which no cause or adequate explanation can be found are often encountered in children. Although these symptoms represent physiologic disturbances which differ widely in kind, increasing knowledge suggests a definite interrelationship and a similar if not a common origin. Barbour, for want of a better name for such a group, called them functional disorders. He fed whole adrenal gland (¼ grain [0.02 Gm.]) to one hundred and fifteen infants suffering from one or more of the symptoms just mentioned and in some cases added ⅛ grain (0.008 Gm.) of thyroid, with gratifying results. No injurious effects followed the administration of either glandular substance. Both the adrenal and the thyroid seemed to be distinctly beneficial to the general health and development of the infants in the series.

WILLIAMSON, New Orleans.

DISCUSSION ON RADIODIAGNOSIS IN DISEASES OF CHILDREN. Proc. Roy. Soc. Med. **27**:1385 (Aug.) 1934.

Dr. Bernard Shires read a paper "Radiodiagnosis in Children," and Dr. C. G. Teall read one entitled "Radiological Appearances of Certain Bone Dyscrasias in Infancy and Childhood." He first discusses at length the osseous changes found by roentgen examination in rickets and congenital syphilis and then passes to the consideration of certain disturbances of the growth of the bone in childhood, such as achondroplasia, chondrodysplasia, osteogenesis imperfecta, osteosclerosis fragilis and xanthomatosis. His paper is accompanied by roentgenograms illustrating each disease. Dr. N. B. Capon, J. F. Brailsford and S. Vere Pearson took part in the discussion.

WILLIAMSON, New Orleans.

FROM THEORY TO PRACTICE IN PREVENTIVE MEDICINE. G. BLECHMANN, Bull. Assoc. internat. de pédiat. prevent. **2**:1, 1934.

Blechmann instituted an inquiry among general practitioners in Paris and its suburbs with a view to discovering to what extent the principles of preventive pediatrics are carried into effect. The following consensus was arrived at:

1. Most physicians are in favor of using B C G. Vaccination against smallpox is generally practiced. Vaccination against diphtheria is more widely employed than formerly, while vaccination against typhus is increasingly popular.

2. In cases of measles the parents themselves ask for injections of convalescent serum. As regards acute diseases, especially influenza, the result of the inquiry is most disappointing. Physicians do not always wear overalls and seldom employ the mask.

3. A large number of expectant mothers of the working class resort to the maternity centers. Houses which are hot beds of tuberculosis are gradually being pulled down.

4. Digestive trouble is still frequent among babies. Rickets occurs in its milder form, with a tendency to adiposity.

It is concluded that there is still a wide gap between present-day practice and the recommendations put forward by the association. AMESSE, Denver.

VITAL STATISTICS IN SPAIN FOR 1933. EDITORIAL, An. de pediat. **1**:377 (June) 1934.

The number of live births was 667,818, or 27.81 per thousand persons (the rate in 1932 was 28.34 per thousand persons). The number of stillbirths was 22,328—3.2 per cent of all the births, or 32.3 stillbirths for each hundred live births (the rate in 1932 was 28.34). The mortality from all causes was 16.44 per thousand persons (this was the figure for 1932 also). The infant mortality rate was 112 deaths for infants under 1 year of age per thousand live infants (this was the figure for 1932 also).

The incidence of diseases per hundred thousand persons for the years 1933 and 1932 was as follows:

	1933	1932
Typhoid	13.58	13.10
Measles	12.49	16.63
Diphtheria	4.92	4.74
Pulmonary tuberculosis	83.62	93.73
Other forms of tuberculosis	24.11	24.84
Bronchitis	78.23	83.06
Pneumonia	164.11	167.09
Diarrhea and enteritis	184.49	189.15
Congenital debility	70.29	70.29

HERRON, Spokane, Wash.

HOMOSEXUAL TWINS. J. SANDERS, Nederl. tijdschr. v. geneesk. **78**:3346 (July 21) 1934.

Six concordant homosexual identical twins, one discordant, perhaps pseudo-homosexual identical twin and one discordant homosexual fraternal twin are described. Sanders concludes that it is highly probable that homosexuality is due to heredity. VAN CREVELD, Amsterdam, The Netherlands

Society Transactions

THIRD INTERNATIONAL PEDIATRIC CONGRESS

Scientific Meetings, London, England, July 20 and 21, 1933

GEORGE F. STILL, M.D., LONDON, ENGLAND, *President*

Thursday, July 20

THE NATURE OF ALLERGY AND ITS RÔLE IN DISEASES OF CHILDREN

EXPERIMENTAL PATHOLOGIC STUDIES ON THE NATURE AND RÔLE OF BACTERIAL ALLERGY. R. ARNOLD RICE RICH, Baltimore.

The term "allergy" is used to designate only that state of specific hypersensitivity which develops as the result of the entry of foreign protein into the tissues and which manifests itself locally by the occurrence of damage to tissue and inflammation wherever the foreign protein or its specific fraction lodges in previously sensitized tissue. The relation between allergy and immunity is discussed. The author separates immunity from allergy in three different types of experiments. First, it was found possible to establish acquired immunity without the concomitant development of allergy by inoculation of animals with syphilis. Second, immunity was separated from allergy by injecting the serum of allergic, immune animals into normal ones. The immunity was transferred to the latter, but not the hypersensitiveness. Finally, immunity was separated from allergy by means of desensitization. In each of these three types of experiments immunity operated in full force in the complete absence of allergic inflammation.

CLINIC OF ALLERGY IN INFECTIOUS DISEASES. DR. FRANZ HAMBURGER, Vienna, Austria.

Various phases of allergy are discussed, such as clinical methods of demonstrating allergy, how soon after infection allergy begins, how long allergy lasts, how it is measured and what factors affect the allergic state. The rôle of allergy in tuberculosis is stressed chiefly, and such problems as the evaluation of the tuberculin reaction in the diagnosis, prognosis, prophylaxis and therapy of tuberculosis are considered. Brief mention is made of allergic conditions in vaccination, syphilis, pertussis, diphtheria, scarlet fever, typhoid fever and dysentery.

CLINICAL STUDY OF NONINFECTIOUS ALLERGY IN INFANCY. DR. MAURICE PÉHU, Lyons, France, and DR. PIERRE WORINGER, Strasbourg, France.

This monograph consists of a detailed presentation of allergic conditions in infancy due to noninfectious agents, such as pollens, epidermal products, dusts, foods, drugs, parasites and physical agents, as heat, cold and light. A short historical sketch of allergy since the word was suggested by von Pirquet in 1906 is presented. Diagnostic methods, including scratch tests, intradermal injections, patch tests, conjunctival and nasal instillations, the reaction of Prausnitz and Küstner, complement-fixation reactions and precipitation reactions are briefly explained. The various allergic manifestations in the cutaneous, respiratory, gastrointestinal and other systems of the body are discussed, and the generally accepted methods of treatment are considered. The article offers nothing new on allergy

but furnishes an excellent compact summary of the present knowledge of this subject with special regard to infants. An extensive bibliography is added.

Friday, July 21

THE PROPHYLAXIS OF MILK-BORNE DISEASES

TRANSMISSION OF DISEASES BY MEANS OF MILK. DR. ALFRED PETTERSON, Stockholm, Sweden.

Of the various diseases transmitted by milk, tuberculosis is undoubtedly the most important. The part played by the bovine bacillus in the total mortality of tuberculosis is comparatively small but still large enough to be serious. Human bacilli may also be introduced into the milk, but the risk of infection with the human type is somewhat less than with the bovine type. Although infection with the bovine type may be comparatively benign, it can also occasionally run a rapid and malignant course. Although the risk of infection with undulant fever is considerable in those districts where infectious abortions occur, children under 10 years of age are only slightly susceptible. The sensitiveness of man to hoof and mouth disease seems uncertain.

Protective measures consist in breast feeding, satisfactory control to insure that the milk is from healthy cows and that it is not contaminated, destruction of pathogenic organisms by heating the milk and proper handling of the milk.

THE SAPROPHYTES OF MILK AND THEIR SIGNIFICANCE. PROF. BESSAU, Berlin, Germany.

The most important of the saprophytes of milk are the colon bacilli. The danger lies in the ingestion of living colon organisms rather than in the decomposition of the milk. This hazard may be avoided by sterilization of the milk or by the feeding of dried milk or buttermilk. Breast milk inhibits the growth of Bacillus coli in the large intestine, but the problem of producing a bifidus-flora with artificial food has not been perfectly solved. Normally the upper sections of the intestine are free from B. coli because of the action of the digestive juices. At times of lowered resistance, however, endogenous coli may spread to the upper part of the intestinal tract. Certain strains of B. coli in themselves may lead to enteritis.

PROPHYLAXIS OF DISEASES DUE TO MILK. PROF. G. B. ALLARIA, Turin, Italy.

This subject was presented from a practical point of view, as it is at present being discussed in Italy, where there is a strong movement for the improvement of the dairy industry, particularly regarding the production of clean milk for infants. The extrinsic and intrinsic factors in milk capable of causing disease are discussed. It is considered more advisable to furnish milk made safe by treatment with heat than to favor the feeding of infants with raw milk, even though it is thoroughly inspected and carefully handled. Rather than pasteurization, the author prefers Stassano's method, by which milk is forced through a space 1 mm. in thickness between concentric tubes of nickel-plated copper several meters long, and heated to 75 C. by water running along the tubes. It is desirable to obtain legislative action to require inspection of dairy farms and herds and supervision of the distribution of the milk by medical health officers.

PROPHYLAXIS OF DISEASES DUE TO MILK. PROF. P. LEREBOULLET, Paris, France.

To obtain raw milk in a perfectly safe condition presents so many difficulties that pasteurization of clean milk is strongly recommended. Safe milk can be furnished only by the most precise hygienic control, which is facilitated by well organized dairy companies and milk depots which represent the principal inter-

mediary between the milk taken from the farm and the milk distributed in the city. The control should be official and should consist of a series of measures by which the milk is watched from the time of milking until it is finally delivered. The milk should be bottled immediately after pasteurization. If proper control of milk cannot be assured, the milk should be boiled before being fed to children. It is highly desirable to undertake a vigorous campaign to improve the general conditions of the production and sales of milk in all countries.

PHILADELPHIA PEDIATRIC SOCIETY

Tuesday, Dec. 11, 1934

JOHN D. DONNELLY, M.D., *President, Presiding*

THE TONSIL AND ADENOID PROBLEM; THE SYSTEMIC INFLUENCE OF INFECTION OF THE UPPER RESPIRATORY TRACT. DR. GEORGE M. COATES and DR. WILLIAM GORDON.

The present knowledge of the anatomy and the physiology of the tonsillar tissues of the upper respiratory tract was reviewed. The opinion that the healthy tonsil helps in immunity, particularly during the early years of life, and that in children under 6 years of age it has a protective function was upheld.

To make the proper diagnosis of tonsillar infection the following are necessary: (1) a careful history and (2) a careful examination of the lymphoid elements of the pharynx. The history of local tonsillar infection, cervical adenitis and other infections often thought secondary to tonsillar infection require a most careful investigation of the lymphoid structures in the pharynx. Findings suggestive of tonsillar tissue infection are: a purplish red tinge to the anterior pillar and pus or cheesy débris exuding from the crypts following pressure, particularly on withdrawing the anterior pillar with a retractor.

The opinions of various authors on the place of the tonsil in focal infection were then outlined. The authors themselves maintained that whether the tonsils and adenoids are responsible in whole or in part for the systemic infection or whether they have no relationship to it, once the fact that they are definitely infected is established they should be removed. They did not wish to go on record as believing that every tonsil is infected, but they could not with any assurance say that a given tonsil is not infected unless that tonsil is removed and subjected to a careful bacteriologic and pathologic examination.

They concluded that when a septic tonsil is discovered in association with some systemic disorder the diagnosis of tonsillar infection as the cause of this disorder can be satisfactorily arrived at only after meticulous study, often repeated if necessary, on the part of the laryngologist and consultation with the attending pediatrician, internist or surgeon.

DISCUSSION

DR. J. C. GITTINGS: The authors' conclusions are eminently safe and sane and will bear reiteration:

(1) A painstaking thorough examination by a laryngologist to determine the presence or probable absence of infection of the lymphatics of the oropharynx and (2) a consultation to determine the relationship, if any, between the lymphoid infection and the systemic disorder of the patient are necessary.

With proper caution the authors stated that operative intervention may give striking results. The inference also is obvious that the good results may not follow.

It always seemed to me somewhat presumptuous that a pediatrician should advise that a patient have a tonsillectomy. Rather should the advice be to consult

a laryngologist and let him decide whether or not operation should be done. On the other hand, no case should be referred to a laryngologist without a verbal or written request for the examination outlining the condition of the patient as (1) likely to be due to focal infection and (2) as an operative risk. For example, no child subject to attacks of cyclic vomiting with ketosis should ever be operated on without the surgeon's knowledge of the potentialities, so that adequate preoperative and postoperative precautions can be taken.

That tonsillectomy should not be done on a child under 5 or 6 years of age, if it is possible to avoid it, is a wise dictum. How often one sees in young children the development of new lymphoid masses along the edge of the posterior pillars and the soft palate several months after tonsillectomy. I have never seen these nodules develop prior to tonsillectomy. It is difficult to escape the conclusion that the organism is endeavoring to replace some of the kind of tissue that has been removed. On the other hand, when infected adenoids block the postnasal space, with consequent interference with sinus drainage and aeration of the eustachian tube, as well as with nasal breathing, an adenoidectomy without tonsillectomy can often be done with profit in the child under 6 years of age.

That the adenoid tissue probably will grow again is no contraindication, as the new growth rarely is excessive and the interval is sufficient to meet the needs. In spite of the fact that tonsillectomy does not prevent colds in the head and recurrences or even occurrences of rheumatic infection and certainly does not prevent chorea, one may take some comfort from the undoubted fact that it does prevent follicular tonsillitis and usually peritonsillar abscess. It is true that one attack of follicular tonsillitis is apt to be followed sooner or later by one or more recurrences. It is also true that, to a child, a tonsillectomy is scarcely more of an ordeal or a danger than an attack of tonsillitis. In removing definitely infected tonsils, therefore, one is probably saving the patient more suffering and possible danger than one is causing.

Finally it may be well to warn against operation too soon after an acute nasofaucial or pharyngeal infection. It is difficult to be didactic about how long one should wait after complete cessation of all signs and symptoms of acute infection before operation, but when one considers the relatively tremendous operative trauma in tonsillectomy, and especially adenoidectomy, with the opening up of countless avenues of absorption, the temptation is to insist on a minimum of three or four weeks. To be on safe ground, one might also demand that a shorter interval could be justified only by a bacteriologic study to determine the absence of any virulent strains of the ordinary pathogens of the nasopharynx.

DR. K. M. HOUSER: Dr. Gittings has graciously passed on to the otolaryngologist the burden of deciding absolutely whether the tonsils shall be removed. It seems to me that there are certain instances in which the opinion of the pediatrician is of more value than that of the otolaryngologist. I am thinking particularly of the patients with recurrent tonsillitis who, if seen six weeks later without the knowledge that these attacks have occurred previously, frequently show nothing, and I believe that under those circumstances the history and the opinion of the pediatrician are worth more than the findings of the otolaryngologist, provided that one accepts recurrent tonsillitis or one attack of severe tonsillitis as one indication for tonsillectomy.

DR. P. NICHOLSON: There is another point of view which has not been touched on. One sees a great many cases of marked undernourishment in children in which thorough and careful examinations and elimination point to the tonsils as a probable focus of infection. When all other possible foci are eliminated the tonsils should be removed. This leads to a very different line of thought as to whether the tonsils should come out, entirely aside from the appearance of the tonsils and previous tonsillar infection. I agree with every word that Dr. Coates has said, as his statements are both conservative and broad-minded. The tonsils are like a sponge, very easily infected, and in all cases of sinusitis with drainage over the tonsils they should be removed. This means that practically 95 per cent of all tonsils will be removed. There are few children who do not have recurring colds;

this is another way of stating that there is sinus infection in a large number of these cases. I had a personal experience myself once which shows the point of view of diagnosis by elimination. For years I suffered from malnutrition and felt extremely tired. After very thorough examination and elimination of other sources of infection I thought that possibly my tonsils were a focus of infection. Eight different nose and throat specialists thought that there might possibly be something there, but could not say so definitely and advised against operation. Finally I went to Dr. Coates and told him that I would like to have my tonsils out regardless, and he removed them. I asked him to have a culture made to tell me whether the diagnosis was correct. After operation, when I asked him if the culture had been made, he said that it was not necessary to make a culture of the tonsils, as he had obtained a half teaspoonful of pus from back of one of them. In one year I gained 25 pounds (11.3 Kg.) in weight. There are a number of such cases in childhood. I have yet to see any serious results following tonsillectomy in children who have been operated on for me, but I have seen remarkable improvement in nutrition.

Dr. George B. Wood: The tonsil has always had a great deal of interest for me, not only because of its clinical importance but also because of its anatomy, embryologic and mature, and its physiology and functional possibilities. From my own experimental research, from the vast amount of published literature concerning its morbidity, it seemed at one time scarcely possible for one to reach adult life with his tonsils still in his throat. However, maturing years bringing with them clinical experience, have made me today a conservative almost to the point of agreeing with certain co-authors who speak of "the massacre of tonsils." as a matter of pure prophylaxis I regard the operation on the tonsils as an unjustifiable procedure. There is such a thing as death due to tonsillectomy; there are such things as serious after-complications, such as pulmonary abscess. They are rare, but are sufficiently frequent, especially when one remembers the less dangerous complications that are more frequent, to make it imperative that there must be some morbid indication for subjecting a child to this mutilation.

On the other hand, there is no doubt in my mind, in any pediatrician's mind or in any otolaryngologist's mind that the removal of tonsils can be not only justified but strongly indicated. Sometimes these indications are plain and distinct, while at other times considerable judgment is necessary to act wisely, and also sometimes one must give the patient the benefit of the doubt and operate without positive indications.

I agree with Dr. Nicholson that the opinion of the family physician forms an important item concerning the advisability of tonsillectomy. Especially must the internist and the pediatrician give the otolaryngologist information concerning not only the general condition of the patient, whether he is suffering from evidences of focal infection, but also report their observations as to previous inflammatory attacks. In the majority of cases the data obtained by inspection of the tonsils are of little importance in comparison with the history.

In a series of from fifty to one hundred tonsils removed as a routine at the Graduate Hospital of the University of Pennsylvania on which a previous careful history was taken and notes made concerning the presence of pus, cryptal contents, color and other features the only consistent item that gave us any preknowledge as to what a subsequent histologic examination would show was the history of recurrent tonsillitis. In nearly all the patients who had a distinct history of several attacks of tonsillitis there were pathologic areas in the removed tonsils on histologic examination.

Recurrent tonsillitis, therefore, to my mind, is one positive indication for removal of the tonsils. Again, I would say that in the majority of cases the local appearance of the tonsils and other clinical data are only circumstantial evidence.

Dr. George M. Coates: This question has caused a great deal of discussion in the last few years. Dean thinks that a great many of these patients have an unrecognized sinus infection at the time of operation or that sinus infection develops

after tonsillectomy. Sometimes sinus infection is caused by tonsillectomy, but not always. In San Antonio the other day, at the meeting of the District 2 American Academy of Pediatrics, Shea of Memphis advanced the thought that as the tonsils are undoubtedly auto-immunizing agents, one of the main purposes of the sinuses is to participate in auto-immunization, so that when the tonsillar half of this mechanism is taken out an undue burden is thrown on the sinuses. This burden the sinuses are not always able to carry, and their resistance is broken down. It seems to me that the need for tonsillectomy lies between those two opinions of Dean and Shea.

In regard to tonsillectomy in children under 5 or 6 years of age, my plan is usually to wait until the child is over 6 years old and then, if adequate cause exists, remove the tonsils. There are plenty of cases, however, in which adenoids must be removed in children under 5 years of age; the sinuses will not develop if there is not proper aeration. In children under 5 or 6 years of age whose tonsils are removed and in whom further lymphoid tissue develops, as Dr. Gittings mentioned, I think that this compensatory hypertrophy is an evidence, as he said, that the patient is not through with his tonsils. Aural infection may be caused by diseased tonsils as well as diseased adenoids, although not as often by the former as by the latter. The tonsils should not be taken out too soon after an acute infection. Dr. Nicholson brought up the question whether the otolaryngologist should submit to dictation. I do not think that he really dictated to me. I do not remember the case, but I suppose that I did as he wished. In cases in which everything else has been eliminated I am perfectly willing to remove the tonsils, if nothing else possibly could be causing the patient's illness. All tonsils are more or less infected, and in certain instances one cannot make the proper diagnosis until the tonsils are out. The opinion of the pediatrician is a large factor in these cases. Repeated attacks of tonsillitis come from diseased tonsils.

Jan. 8, 1935

JOHN D. DONNELLY, M.D., *President, in the Chair*

PREPARATION OF DRY LYOPHILE SERUM. DR. EARL W. FLOSDORF.

The preservation of serum by drying was attempted by Erhlich, and methods for accomplishing it have been improved subsequently by various workers. The present method and apparatus permit the drying of the serum from the frozen state without loss of sterility, without biologic, chemical or colloidal alteration and in quantities and in containers usable by the clinician. The serum is initially rapidly frozen in the final containers at -75 C. The containers are then immediately attached in large numbers by high-vacuum tight connections to the manifold that opens into a suitable condenser maintained at -75 C. by carbon dioxide snow ethylene glycol mono-methyl ether. By means of a pump the air is quickly exhausted down to a pressure of from 0.02 to 0.1 mm. of mercury.

The size and shape of the serum container are such that the input of heat from the atmosphere at the surface of the glass and the output of heat due to the evaporation of water at the surface of the serum under the high vacuum maintain an equilibrium temperature of the serum well below its freezing point until dry, the ice subliming over to the very cold condenser, the region of lowest vapor pressure. No other external cooling of the serum is required to keep it frozen. The bore of the exhaust tubes from the containers must be large to permit the escape of the large volume of vapor (highly expanded at the low pressure). With the correctly shaped container twenty-two hours are sufficient for the serum to lose 99.9 per cent of its water. The glass exhaust tube can be sealed with a special torch, so that the container may be removed with its contents preserved under vacuum and sterile.

The container has a rubber stopper with a thin membrane section easily punctured by a syringe needle. The vacuum pulls in the water from the syringe in an amount equal to or less than 25 per cent of the original amount, as desired by the clinician. Dissolution is very rapid (from one-half to five minutes), yielding a clear fluid.

Relative Stability of Dried Serum and Lyophile Serum. Dr. H. Eagle.

DISCUSSION

Dr. Stuart Mudd: The antecedents of the work on the apparatus by Dr. Flosdorf came from both the clinical laboratory and the biologic supply house. Dr. Elser, in charge of the laboratory of the New York Hospital, had been at work for twenty-five years and had carried the process to a very considerable degree of achievement. The procedure of drying serum from the frozen state was advanced a considerable degree further by Dr. Reichel and his associates at Glenolden.

To the clinical and experimental laboratories there are many advantages in being able to preserve diagnostic, preventive and curative serums without alteration over long periods. Distribution and storage of commercial serums also should be facilitated, and loss of value and ultimate wastage due to deterioration should be reduced to a minimum by this procedure.

One of the most interesting uses of the process is that it makes possible the utilization of human serums for the prevention and treatment of illness widely removed in time and space. Thus, scarlatina or measles convalescent serum might be collected in one epidemic and used elsewhere years later. We have vaccinated medical students against typhoid, titrated their serums and collected them at the optimum time. These serums are preserved and stored until needed for treatment. We are also particularly interested in collecting convalescent serums in epidemics of obscure etiology, for instance, in outbreaks of the encephalitides and of epidemic "influenza." Such serums may be of invaluable aid in determining the etiology and interrelationships between epidemics in different localities occurring at different times.

The opportunity afforded by this process for harvesting human serums when available and using them when needed gives a great stimulus to the development of serum centers for the collection and distribution of human serums. Human serum centers are operating in Paris, Stockholm, Detroit, Chicago, Providence, R. I., and Milwaukee. Under the stimulus of these and feeling the clinical need for a similar center, the departments of bacteriology and of pediatrics have established a serum center in Philadelphia. Dr. McGuinness will speak of the results of its first year of operation.

Clinical Use of Lyophile Serum. Dr. Aims McGuinness.

The value of convalescent and pooled adult human serums in the prophylaxis of measles, mumps, chickenpox and scarlet fever is of established value. The therapeutic use of convalescent scarlet fever serum and convalescent mumps serum in the treatment of those two diseases has had favorable reports.

The development of the lyophile process facilitates the preservation and storage of human serums. To take advantage of this process the Philadelphia Serum Exchange has been established at the Children's Hospital.

In the course of the past ten months the exchange has collected, lyophilized and dispensed the following types of serum: (1) pooled adult (human) serum; (2) convalescent serum of measles, mumps, chickenpox and scarlet fever; (3) umbilical cord serum; (4) antistaphylococcic and antityphoid serums.

Lyophilized serums have been used in the treatment of 3 patients with scarlet fever, 2 patients with typhoid fever and several patients with streptococcic septicemia, with favorable results.

DISCUSSION

Dr. Pascal F. Lucchesi: The use of convalescent serum in the treatment and prevention of contagious diseases has been known for some time. All types of convalescent serums have been used, chiefly, however, to prevent disease. Therefore, the use of convalescent serum is not new. Lyophile serum is convalescent serum but is prepared differently. From the point of view of the hospital, the greatest value of this serum is in its prophylactic use. Since it can be preserved for a great length of time, it would be of great help in the prevention of cross-infections in hospitals for contagious diseases and in children's wards, orphan asylums and other institutions of this type. As for its use in the treatment of contagious diseases, its value at present is doubtful. Not many patients have been treated as yet, and therefore no definite opinion can be reached. In my own experience with the use of convalescent serum in the liquid form, I should say that it has been unsatisfactory. At present I am attempting to study a series of cases in which the patients were treated with scarlet fever convalescent serum.

Another question which may be raised is how long passive immunity resulting from the use of this serum lasts. It is known that liquid convalescent serums give an immunity which does not last longer than two or three weeks. This point has not yet been determined for the use of lyophile serum.

With reference to reactions, Dr. McGuinness has already pointed out the particular type of reaction that might be expected. There is nothing that I might add to this.

I am glad to have been of service to Dr. Stokes, Dr. Mudd and Dr. McGuinness in their preparation of this serum. I understand that serum centers already established in Chicago and Detroit have been successful, and there is no reason why a serum center cannot be just as successful in Philadelphia.

Dr. Joseph Stokes Jr.: In serum centers, fluid serum might be considered the checking account and lyophile serum might be considered the savings account.

One sees the possibility of an ever-widening field for developing in adults highly immune and hyperimmune serum which can be processed and made useful in the treatment and prevention of many diseases.

The Philadelphia Serum Exchange is a nonprofit organization. There is a certain amount of money that is necessary for payment of donors. The exchange is available for the use of physicians throughout the city.

Factors Influencing the Use of Immune Globulin (Human Placental Extract). Dr. Charles F. McKhann, Boston.

Placental extract can be prepared in large amounts and can be made available for the prevention or modification of measles on a large scale. Attempts to refine and concentrate the measles antibody have resulted in preparations of less potency than the extracts containing all the globulins. However, the refined preparations can be passed through Berkefeld filters and may therefore be deemed safer to use.

The results in a series of 1,258 cases demonstrate that the refined extracts, although less active than the crude preparations, are still effective in the prevention or modification of measles. However, this number of tests is inadequate to permit the determination of the best fraction of the extract to use and the dose required for children of various ages and at various stages of the incubation period of the disease.

The scarlet fever and diphtheria antibodies in placental extract appear to be almost entirely in the pseudoglobulin fraction, whereas the measles and poliomyelitis antibodies appear to be distributed throughout several protein fractions. The tissue protein insoluble in acidified salt solution contains no diphtheria antitoxin but does contain the antibody neutralizing the poliomyelitis virus. It has not been tested for activity against measles.

Reactions following the injection of placental extract, although infrequent, appear to be due in some measure to the inclusion in the finished extract of

variable amounts of a specific tissue protein. A method of preparation and administration of extract to eliminate reactions is at present under investigation.

DISCUSSION

DR. CHARLES F. MCKHANN, Boston: I am glad that the item of cost has been brought up. What the commercial houses do with this preparation is beyond our control, in accordance with the ruling of Harvard University which prohibits their medical school from making any profit from, or controlling, a preparation of this type. Neither do we have any direct control of whether the commercial product is good or bad. As regards Massachusetts, this preparation is being manufactured by the state antitoxin laboratory and will be distributed throughout the state free of charge to any physician who desires to use it and who sends in a report of the results obtained. This has been extended to include all members of the New England Pediatric Society. This year we expect to make up 10,000 doses of measles serum in cooperation with the Massachusetts Department of Public Health Antitoxin and Vaccine Laboratory.

The dosage is based on the nitrogen content of the finished lot. At present each lot is made from 50 or more placentas.

Book Reviews

The Principles and Practices of Medicine. By Sir William Osler. Revised by Thomas McCrae. Price, $8.50. Pp. 1196, with 22 illustrations. New York D. Appleton-Century Company, Inc., 1935.

The continued popularity of Osler's "Principles and Practice of Medicine" is well established, and the recently published twelfth edition should increase it.

The customary simple, concise plan is followed, and the material is well presented in the new type face which, while permitting more words per page, is easily read. The book opens with the familiar discussion of typhoid fever. This disease is not common enough to deserve this prominent position, but the discussion serves as an admirable example from which the plan of presentation of other diseases is derived.

McCrae mentions the difficulty of selecting the points of permanent value from the mass of material available. However, the changes since the eleventh edition which are present throughout the book show a careful and sane selection.

The continued use of British statistics in the presentation of disease incidence is probably not as intelligible to American students as it might be, but is justified by the greater accuracy of such figures than comparable ones from the registration area of the United States.

The clear and brief presentation without sacrifice of any facts of importance, will continue to make this text one of the most if not the most valuable book for the student and practitioner of medicine.

Child Psychiatry. By Dr. Leo Kanner. Price, $6. Pp. 527. Springfield, Ill.: Charles C. Thomas, Publisher, 1935.

Kanner covers the whole field of child psychiatry and the related field of child neurology. Personality disorders are described in a broad and comprehensive manner. Neurologic conditions are discussed only as they must be included in the general picture of behavior.

The book is divided into two parts. The first discusses in a general way mental hygiene, clinic methods and attitudes. Part two describes the organic conditions of the central nervous system, glandular conditions briefly, signs and symptoms of personality disorders in children and the correct attitude to be assumed toward the various conditions.

Kanner takes an objective attitude. He describes behavior disorders accurately and gives the general etiologic factors back of them. The psychoanalytic attitude is rather violently rejected. The book is on a "common sense"—often superficial—basis. The material is presented in an interesting manner. The book can be recommended as a safe, conservative, introductory text to the psychiatry of childhood.

Methods and Materials of Health Education. By Jesse F. Williams, M.D., and Fannie B. Shaw, M.A. Pp. 331. New York: Thomas Nelson & Sons, 1935.

This splendid small volume should fill a gap in an important field of work which is becoming slowly but surely recognized as a fundamental branch of education.

Williams and Shaw have succeeded in presenting in a simple and clear fashion methods and materials of health education that should be welcomed especially by physicians, teachers and members of groups interested in child study. They classify and define the various terms used in health education and then follow with chapters dealing with the nature of the child, health service, health instruction, materials for teaching health and tests and measurements in health educa-

tion. The closing chapter, dealing with the health of the teacher, stresses the importance of this matter and elaborates the various factors involved. Each chapter is followed by questions for study and discussion, enhancing greatly the value of this book as a text.

Nutrition Work with Children. By Lydia J. Roberts. Price, $4. Pp. 639, with 18 illustrations. Chicago: the University of Chicago Press, 1935.

Roberts has thoroughly revised this standard work on nutrition. In chapter 3, on the methods of judging nutrition, considerable has been added, particularly the studies of the Children's Bureau; Dublin, Gebhart and Clark's studies, and Lucas and Pryor's work on the width-length index. In the sixth chapter, on the causes of malnutrition, parts have been added on the effect of the depression on nutrition and health, and a summary of the studies on the effects of optimum versus adequate nutrition is given. An entire chapter has been added on the mental effects of malnutrition, and the parts on health agencies and parent education have been greatly expanded.

The first edition of this book was a remarkable work, and the second edition has brought the field of nutrition up to date. This is by far the best work that has appeared on this subject and should be read with profit by every pediatrician. It is beautifully printed and well bound.

Preventive Medicine and Hygiene. By Milton J. Rosenau. Price, $10. Pp. 1480, with 147 illustrations. New York: D. Appleton-Century Company, Inc., 1935.

This is the sixth edition of this well known standard textbook. New material has been added to the sections on tuberculosis, diphtheria, Vincent's angina, insect-borne diseases and quarantine, and the parts on venereal diseases, sex hygiene, heredity, eugenics, deficiency diseases and occupational diseases have been rewritten. New subjects considered for the first time are contraception, maternal mortality, heart disease, diabetes, ringworm, snake poisoning, psittacosis, periodic health examinations and hospitals. It is unnecessary to eulogize such an excellent text-book; the work speaks for itself. This new edition brings the field of preventive medicine entirely up to date in the well written manner begun in the first edition. The book should have a place in every physician's library.

The Cosmic Way to True Civilization Through Parenthood. By George H. Donahue, M. D. Leather. Pp. 68. Northport, N. Y.: Edward Thompson Company, 1935.

The scientific findings and observations that have developed into the present-day knowledge are reviewed and used as a background to develop the author's conclusions that "If there can be awakened in humanity the Will to establish True Civilization, that Will must become centered on the parenthood and childhood of the world. Having so focused attention on this only possible way to achieve this supreme result, parents, teachers, governments, and all human beings will look to succeeding generations to carry the enhancement of life to high and ever higher goals of achievement."

The book is very well bound and printed.

Orthopedics for the Teachers of Crippled Children.—By S. W. Boorstein. Price, $1.50. Pp. 120. New York: Aidem Publishing Company, 1935.

The subject matter treated in this text should be of genuine interest to the teachers of crippled children, especially since it includes valuable references to the best current books and literature on orthopedics. It contains essentially a good outline of the range of cases treated by the orthopedic surgeon and offers

helpful suggestions for the teacher who of necessity should be acquainted with the special problems of a crippled child. The format could be improved, and the book lacks the smoothness and style of a complete text, as do all compilations of lectures.

Erbbiologie der angeborenen Körperfehler. By Prof. Dr. Max Lange. Paper. Price, unbound, 9.60 marks; bound, 11.20 marks. Pp. 143, with 46 illustrations. Stuttgart: Ferdinand Enke, 1935.

The author of this interesting little book was head of the orthopedic outpatient department at Munich and has used this wealth of material for the study that he has undertaken. He believes that practically all the common congenital deformities, namely, those that deal with variations in the bones and joints and extra digits, are due to an inherited tendency, and each of his observations is accompanied by a family tree to illustrate this. The subject matter is very interesting and well brought out. The plates illustrating the various types of deformities are well done.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

FOREIGN

British Paediatric Association

President: Dr. Hugh Thursfield, 84, Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31 A, Weymouth St., London, W. 1.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1, Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Horton R. Casparis, Vanderbilt University Hospital, Nashville. Tenn.
Secretary: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Place: Kansas City, Mo. Time: May 11-15, 1936.

American Academy of Pediatrics

President: Dr. Henry Dietrich, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

American Pediatric Society

President: Dr. Fritz B. Talbot, 270 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. C. F. McKhann, Children's Hospital, Boston.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. L. Howard Smith, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Morris Bridgeman, Children's Clinic, Portland, Ore.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Secretary: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. J. W. Britton, 931 Noble St., Anniston.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. Morgan Smith, 625 Beech St., Little Rock.
Secretary: Dr. Madeline A. M. Melson, 2111 N. Spruce St., Little Rock.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. S. J. McClendon, 2001 Fourth Ave., San Diego.
Secretary: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Place: Coronado. Time: May 25-28, 1936.

GEORGIA PEDIATRIC SOCIETY

President: Dr. William Willis Anderson, 478 Peachtree St., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta, December 1935. Savannah, June 1936.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. Louis H. Segar, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Charles James Bloom, 3439 Prytania St., New Orleans.
Secretary-Treasurer: Dr. J. A. Crawford, 834 Ryan St., Lake Charles.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.
Place: New York City. Time: April 27-29, 1936.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.

Mississippi State Pediatric Society

President: Dr. R. E. Wilson, 205 S. Harvey St., Greenville.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. J. R. Ashe, 306 N. Tryon St., Charlotte.
Secretary: Dr. R. A. Moore, 306 N. Tryon St., Charlotte.
Place: Pinehurst. Time: May 6, 1936.

Oklahoma State Pediatric Society

President: Dr. Julian Feild, 610 S. Monroe St., Enid.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.

Pennsylvania Medical Society, Pediatric Section

Chairman: Dr. Joseph Stokes, Children's Hospital, Philadelphia.
Secretary: Dr. Theodore O. Elterich, 310 Medical Arts Bldg., Pittsburgh.

South Carolina Pediatric Society

President: Dr. William Weston Jr., 1428 Lady St., Columbia.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

Tennessee State Pediatric Society

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Memphis. Time: April 1936.

Texas Pediatric Society

President: Dr. C. O. Terrell, 813 Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.

Virginia Pediatric Society

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

Bronx Pediatric Society

President: Dr. Harry M. Shapiro, 1882 Grand Concourse, New York.
Secretary: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. W. F. Watton, 240 Berkeley Pl., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. A. Levinson, 30 N. Michigan Ave., Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Harris County Pediatric Society

President: Dr. Byron P. York, 3820 Fannin St., Houston, Texas.
Secretary-Treasurer: Dr. E. O. Fitch, 3717 Main St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month. 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

LOS ANGELES COUNTY MEDICAL ASSOCIATION, PEDIATRIC SECTION

President: Dr. George P. Laton, 1136 W. 6th St.
Secretary-Treasurer: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND THE ACADEMY OF MEDICINE OF BROOKLYN, PEDIATRIC SECTION

President: Dr. Charles F. Fisher, 756 Eastern Parkway, Brooklyn.
Secretary: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144, 38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwaukee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Béla Schick, 17 E. 84th St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.
Secretary: Dr. A. V. Stoesser, University Hospital, Minneapolis.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. George J. Feldstein, 3401 5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Tuesday, alternate months from October to April, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Samuel A. Anderson Jr., 2326 W. Grace St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

ROCHESTER PEDIATRIC SOCIETY

President: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Secretary: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. J. V. Cooke, St. Louis Children's Hospital, St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Daniel Budson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (NEW YORK)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, Oct., Dec., Feb. and April.

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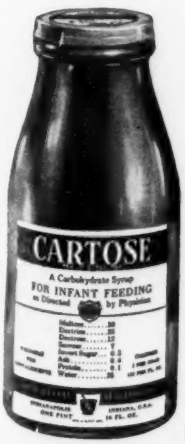

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MERRELL-SOULE Powdered Protein Milk (cultured) was first manufactured in 1919 at the request of a leading pediatrician who sought a more convenient, more uniform, and more stable preparation of the Finkelstein *eiweissmilch*.

Sixteen years have passed during which this now standard Merrell-Soule product has built a brilliant record of performance in the treatment of summer diarrhea and chronic intestinal indigestion (celiac disease).

THESE ARE REASONS WHY

It is easily and quickly reliquefied in the home.
It is uniform in composition and texture.
The finely divided curd does not block nipple holes.
More palatable and, therefore, better taken, especially by the older infant.
It is economical—no waste.

Additional information and a trial supply will be gladly sent upon receipt of coupon.

THE BORDEN COMPANY, Dept. 287, 350 Madison Ave., New York, N. Y.
Please send me literature on Merrell-Soule Powdered Protein Milk (cultured) and a supply for clinical trial.

Name..... M.D.

Street.....

City..... *State*.....

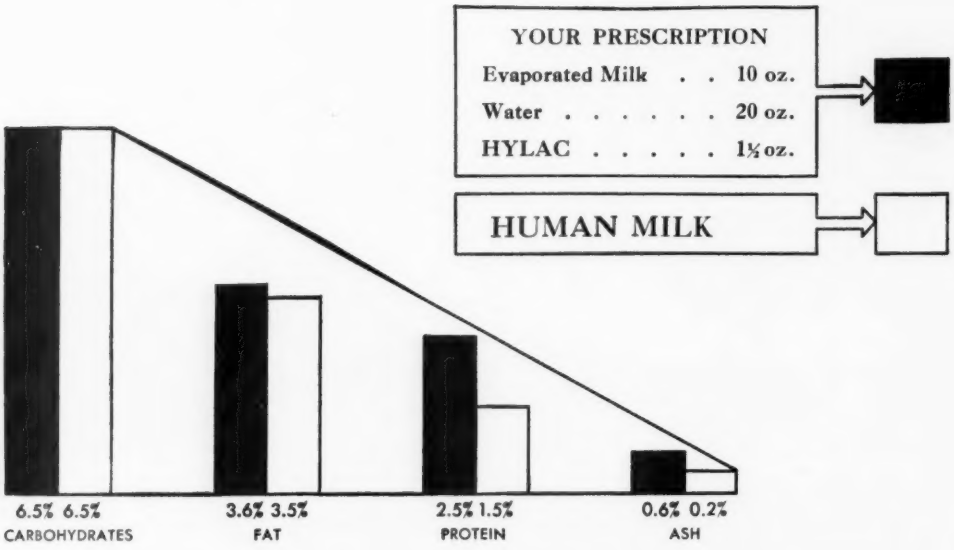
ACCEPTED AMERICAN MEDICAL ASSN. Committee on Foods

Comparing

HUMAN MILK—NATURE'S OWN BALANCED RATION

with

Your Own Prescription of Evaporated Milk with HYLAC



Healthy normal growth requires a *balanced* ration

Hylac is the only available modifier which increases both the milk fat and the sugar content of diluted whole milk so as to provide formulas approximating normal human milk in percentage of milk fat, protein and carbohydrate

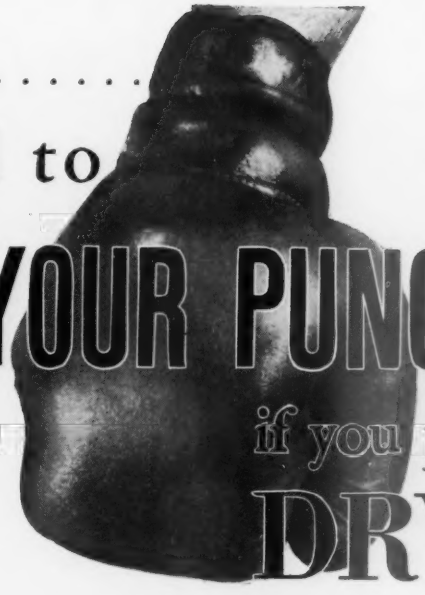
Hylac has been accepted by the Committee on Foods of the American Medical Association

Samples and literature will be supplied to Physicians on request

NESTLÉ'S MILK PRODUCTS, INC. • 155 E. 44th St. • *Dept. H111* • New York, N. Y.

Where Digestive Limitations Exist . . . . . .

no need to "PULL YOUR PUNCHES"



if you prescribe DRYCO

"THE PHYSICIAN, *with a profound respect for the digestive disturbances that may already exist, and fearful of causing more, is apt to delay too long in increasing the strength of the feeding.*"*

In most feeding situations where formulas are weakened, the dangers of underfeeding can be avoided with DRYCO. More digestible, modified DRYCO feedings can be safely fed at 40 to 50 calories per pound within a week of their introduction. More easily assimilable, there is less metabolic waste and, consequently, greater utilization of food.

Furthermore, the ample protein content of DRYCO feedings is an effective safeguard against inadequate supply of this tissue-building element.

● The new DRYCO infant feeding schedule gives separate, concise formulas for the undernourished and the difficult feeding case, as well as for the newborn, the partially breast-fed, or the normal, well baby. Send coupon to receive copies.

* *Dennett*

DRYCO is made from superior quality milk from which part of the butter-fat has been removed, irradiated by the ultra-violet ray, under license by the Wisconsin Alumni Research Foundation (U. S. Pat. No. 1,680,818) and then dried by the "Just" Roller Process.

THE DRY MILK CO., Inc., Dept. DCH, 350 Madison Ave., N. Y. C.

Please send copies of new DRYCO Infant Feeding Schedule.

Name ..... *M. D.*

Street .....

City ..... *State* .....

Check here to receive samples of DRYCO ☐

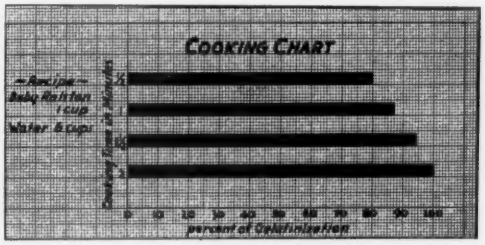
Baby Ralston

COOKS IN TWO MINUTES

The chief values of cereal cooking are assumed to be sterilization, gelatinization and possible increase in palatability. It is an accepted fact that during the cooking process a chemical reaction takes place between the cereal starch and the water, producing gelatinized starch—an hydration product. Gelatinized starch exposes more surface to, and is more quickly acted upon by the enzymes of the digestive tract. Therefore, *the cooking process is completed when complete starch gelatinization has occurred.*

The Ralston Purina Research Department has developed a method (1) for distinguishing between raw and gelatinized starch. This method makes it possible to know, definitely, how well or how poorly certain cereals are cooked.

The graph, herewith, shows results obtained when Baby Ralston is cooked by this method for various periods of time. Note that complete gelatinization occurs in 2 minutes of active boiling in a single boiler over an open flame.



Where long cooking is preferred, Baby Ralston may be cooked for 15 minutes in a single boiler—or 60 minutes in a double boiler without measurable depreciation in vitamin B, providing proportions of water and cereal recommended on the package are used.

Baby Ralston—Research Laboratory Report

Baby Ralston is a smooth, highly palatable and well tolerated cereal composed of wheat endosperm and wheat embryo—fortified with added iron and calcium salts. Because it's so easy to prepare—so delicious that baby takes it eagerly—mothers thank you for including Baby Ralston in the infant's diet. We will gladly send you samples of Baby Ralston—and a copy of the Laboratory Research Report. Simply fill in the coupon, or attach it to your prescription blank.

(1) *Cunningham N. T. The Cooking of Cereal Porridges: Jrl. of Cereal Chemistry 8:403—1931*

RALSTON PURINA COMPANY, Department DC
341 Checkerboard Square, Saint Louis, Missouri

You may send me sample of the new Baby Ralston for testing; also copy of Laboratory Research Report on Baby Ralston.

Name_____ M.D. Address_____

City_____ State_____

FOR *Group* OR *Individual* TREATMENT

The Eveready Professional Model Carbon Arc Lamp is designed for individual treatment. Standard applicators can be attached to this lamp where the use of localized treatment is indicated.

EVEREADY CARBON ARC SOLARIUM UNITS AND PROFESSIONAL MODEL CARBON ARC LAMPS

provide therapeutic radiation of flexible character and uniform intensity

EVEREADY Carbon Arc Lamps afford a choice from five types of therapeutic radiation. With Eveready Sunshine carbons, and using the filter panels of ultra-violet transmitting glass supplied with each lamp, they provide close duplication of natural sunlight. With Eveready Therapeutic "C" carbons, they provide powerful ultra-violet radiation which produces an erythema after brief exposure. Three other types of Eveready Therapeutic carbons emphasize specific bands of therapeutic radiation. Removal of the filter panels permits the use of ultra-violet of wave lengths shorter than those found in natural sunlight.

✓ It is not necessary to use ultra-violet meters with these carbon arcs. There is no aging. Full strength is immediately available. Motor driven, constant current arc control keeps the output from a given type of carbon always the same.

·EVEREADY· CARBON ARC *Solarium* UNITS

PROVIDE RADIATION EQUIVALENT TO AVERAGE CLINICAL SUNLIGHT

Type C7B Four-Arc Unit—For adult groups up to twenty-five
Type C5A Two-Arc Unit—For adult groups up to fourteen
Type C4B One-Arc Unit—For adult groups up to ten

AMERICAN COLLEGE OF SURGEONS

Accepted by the Council on Physical Therapy of the American Medical Association

NATIONAL CARBON COMPANY, INC.
Carbon Sales Division, Cleveland, Ohio
Unit of Union Carbide UCC and Carbon Corporation
Branch Sales Offices • New York • Pittsburgh • Chicago • San Francisco

GERBER PRODUCTS ARE NOT ONLY GOOD

...they're economical

Naturally, the quality and usefulness of any product are your first consideration in recommending it. But we believe that practically every physician is interested in knowing that the product of merit is conveniently and economically available to his patients.

When Gerber's Strained Foods were first introduced, similar products were selling at 20c to 30c for 4 to 5 ounces. Confident that broad markets could be developed that would reduce production costs, we advertised Gerber Products widely and introduced them at 15c for the 4½-oz. can.

This saving meant that more mothers could use Gerber's—more babies could have the benefits of these highly nutritious foods. Through the succeeding years continued promotion has so increased Gerber volume that we have twice lowered prices still further. Today Gerber's may be purchased at 10c a can or less in practically every market.

At the same time we have been able to develop still finer quality. The most recent improvement is the exclusive Shaker-Cooking, which shortens cooking time and eliminates overcooking of outer contents of the can.

We would like to have you examine for yourself the improvement in color and flavor that results from this "stirring" process, which secures heat penetration at the center of the can in 50% to 60% less time than in "still cooking." For free samples, mail coupon below.

• • •

Strained Vegetable Soup . . Tomatoes . . Green Beans . . Beets . . Carrots . . Prunes . . Spinach . . Peas . . 4½-oz. cans. • *Strained* Cereal . . 4½-oz. and 10¼-oz. cans.

Gerber's

Shaker-Cooked Strained Foods

GERBER PRODUCTS COMPANY, DC 8
Fremont, Michigan
(In Canada: *Grown and Packed by* Fine Foods of Canada, Ltd., Tecumseh, Ont.)

Please send me samples of your new-process Shaker-Cooked Strained Foods.

Name.....

Address.....

City.....*State*.....

Why THE KARO BABY AIDS THE DOCTOR

● Every mother craves the best for her baby. She prefers a capable, experienced physician for the baby's supervision, seeks select foods for his regimen, strives for his superior care. Whatever her station in life, her maternal devotion means sacrifice for her baby . . . . . But when the family means are limited, that sacrifice may be at the expense of the doctor. His fee may be disbursed for expensive baby foods, while the baby is taken to a free clinic. Thus, it behooves the family physician or the pediatrician to recommend Karo,* the economical milk modifier. It contains the maltose-dextrin every budget can afford. The baby thrives. The mother saves—but not at the expense of the private physician. Doctor be wise—prescribe Karo for the baby.

*essentially dextrins, maltose and dextrose with a small percentage of sucrose added for flavor

ARE THESE GOOD REASONS?

1. Because rickets has been widely prevalent among infants and children in spite of the prescription by physicians of antirachitic sources;

2. Because it is possible to create in milk a supply of vitamin D sufficient to prevent rickets in the normal child who consumes a normal quantity of milk so enriched;

3. Because Pet Milk is widely used as milk for infants and children on account of its sure safety, uniform richness and more ready digestibility;

4. Because we could enrich Pet Milk with vitamin D without increasing its cost to the public—

FOR those reasons we irradiate Pet Milk with ultra-violet rays, thus enriching it with vitamin D.

A pint of Pet Milk so enriched, diluted with an equal part of water to make a full quart of extra-rich milk, contains vitamin D equivalent to 135 U. S. P. units of the vitamin D of codliver oil—a sufficient quantity to prevent rickets in the normal child.

For young infants, additional sources of vitamin D may be needed for the best growth. For the normal child past early infancy who has daily a minimum of one and one-half pints of whole milk (Pet Milk diluted with an equal part of water), there is in Pet Milk a sufficient supply of vitamin D.

We'll be glad to send samples of Irradiated Pet Milk, a book prepared especially for physicians and a pad of prescription blanks for your use in prescribing Pet Milk.

PET MILK COMPANY
Furnishes no Formulae to the Laity

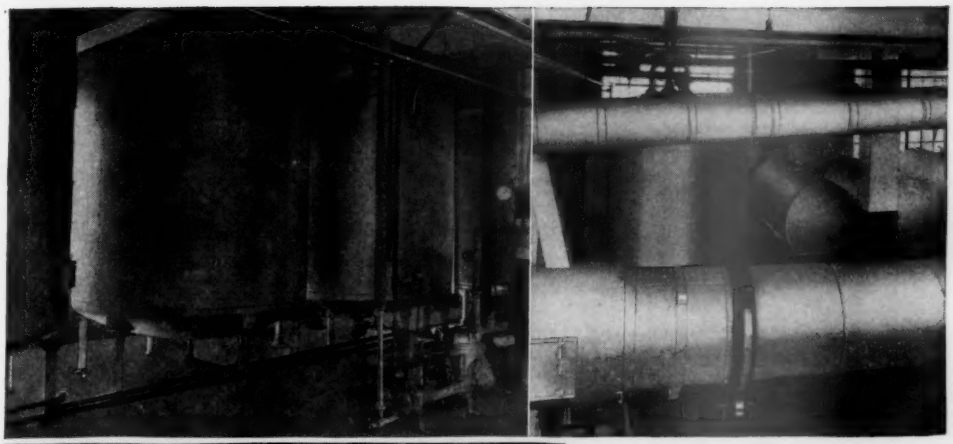
PET MILK COMPANY, 1441h Arcade Bldg., St. Louis, Mo.

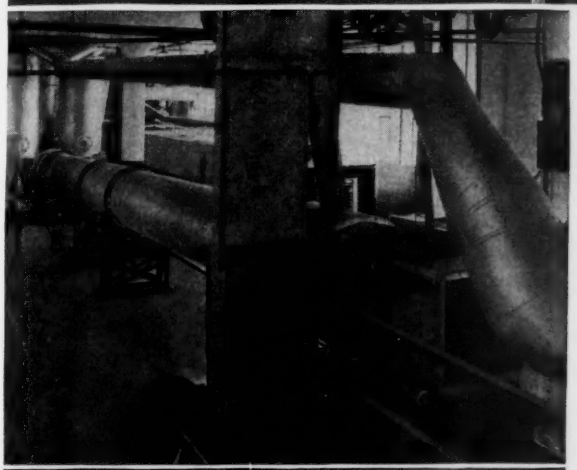
Please send me, free of charge, ☐ **Samples of Irradiated Pet Milk** ☐ **Book for physicians "Irradiated Pet Milk—Its Character, Quality and Usefulness in Infant Feeding"** ☐ **Pad of prescription blanks**

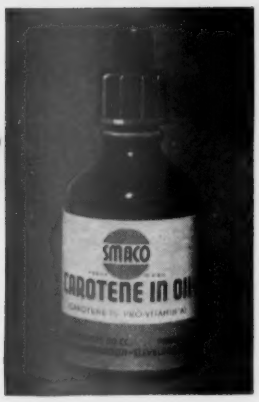
*Dr.*_____ *Address*_____

*City*_____ *State*_____

(Please attach your prescription form or letterhead to this coupon. Offer is limited to residents of Continental U. S.)







Smaco Carotene (Pro-Vitamin A) is offered in drop and capsule form, plain and combined with the Vitamin D concentrate developed in the laboratories of and controlled by Columbia University. Large scale equipment and the finest engineering practises are used in the production of Smaco Carotene in quantities sufficient to meet the demand.

S. M. A. CORPORATION • CLEVELAND, OHIO

"Prevention and cure of teeth and bone deficiencies are the principal purposes underlying the widespread interest in adding vitamin D to milk. Rickets, a common and serious bone weakness developing in infancy and early childhood, can be prevented or remedied promptly by means of this vitamin, and a large percentage of children do not derive the needed amount of vitamin D from ordinary food, especially when they are deprived of sufficient sunshine."—WISCONSIN STATE BOARD OF HEALTH BULLETIN, January-March, 1935.

THE ANSWER TO A NEED

The irradiation of Carnation Evaporated Milk, adding a vitamin D potency sufficient to prevent rickets in the average normal infant, is a step predicated on a long series of observations by the medical profession of the prevalence of rickets and the lack of vitamin D in common foods. . . . Irradiated Carnation Milk is a dependable source of this vitamin—universally available, and so economical that no section of our population need now be deprived.

Irradiated Carnation Milk possesses the following vitamin D potency: 8.4 U. S. P. vitamin D units per fluid ounce; 270 units per quart in undiluted form; 135 units per reconstructed quart when diluted 1 to 1 with water. The vitamin D in 37 fluid ounces of Irradiated Carnation Milk is equivalent to that contained in one teaspoonful of U. S. P. minimum-standard cod-liver oil.

CARNATION COMPANY

Milwaukee, Wisconsin Seattle, Washington

IRRADIATED

Carnation Milk

"FROM CONTENTED COWS"

WRITE FOR "Simplified Infant Feeding," a new and authoritative publication for physicians

Here are the answers, DOCTOR

to some special questions you've been asked about the FEEDING OF YOUNG INFANTS

1. How early can cereal be given to the normal infant?

2. What cereal can help to prevent the anorexia which frequently develops during the sixth month when the "bottle diet" is no longer adequate?

3. How are extra quantities of valuable minerals—iron, phosphorus and calcium easily introduced into the infant's diet?

1. Because of its lack of irritating cellulose, Baby Ralston may be added to the dietary of a normal infant as early as three months.

2. Because it is a specially designed infant cereal, rich in vitamin B, one daily serving of Baby Ralston (16 grams dry) should contribute toward preventing the anorexia and malnutrition, due to insufficient amounts of vitamin B, which are frequently met with after the sixth month, when the "bottle diet" is no longer adequate.

3. By means of daily portions of Baby Ralston, a natural, highly palatable cereal composed of wheat endosperm and wheat embryo enriched with iron, phosphorous and calcium salts.

We will gladly send you samples of Baby Ralston, the palatable, quickly cooked cereal for infants. Also a copy of the Research Laboratory Report. Simply use the coupon.

Wheat endosperm and wheat embryo, fortified with extra calcium and iron.

BABY RALSTON

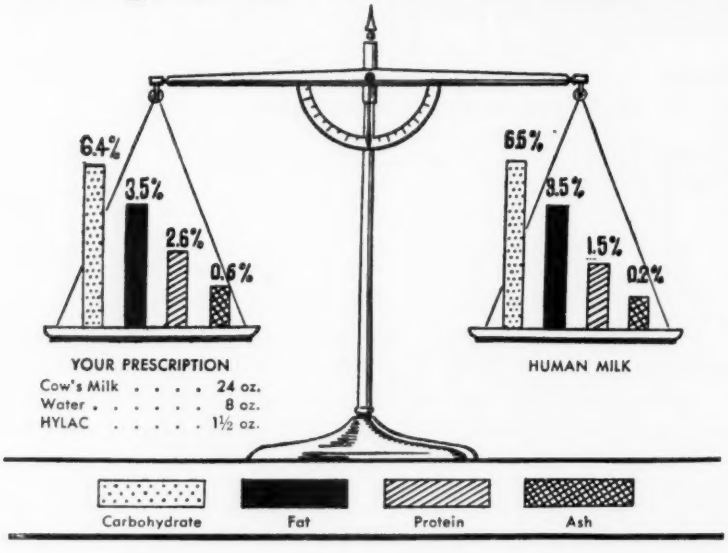
RALSTON PURINA COMPANY
Department DC, 204 Checkerboard Square, St. Louis, Missouri

You may send me samples of the new Baby Ralston for testing; also copy of Research Laboratory Report on Baby Ralston.

*Name*_____ *M. D. Address*_____

*City*_____ *State*_____

Your own Prescription
Compared with Human Milk



Practically Identical
in their proportions of food substances

Hylac is the only available modifier which increases both the milk fat and the sugar content of diluted whole milk so as to provide formulas approximating normal human milk in percentages of milk fat, protein, and carbohydrate.

One Tablespoon	=	25 Calories
One Ounce (6 Tablespoons)	=	150 Calories

Hylac is a spray-dried mixture of malted whole wheat extract (essentially dextrins and maltose) with homogenized cow's milk, added milk fat and milk sugar and a small amount of iron citrate.

Samples and literature will be supplied to Physicians on request.

Hylac has been accepted by the Committee on Foods of the American Medical Assn.

NESTLÉ'S MILK PRODUCTS, Inc.
155 East 44th Street, Dept. H103, New York City

Announcing . . .

The NEW ·EVEREADY· Professional Model Carbon Arc Lamp Model A-2

INCREASED ULTRA-VIOLET INTENSITY

A powerful, flexible and highly efficient source of therapeutic radiation for the physician's office

A NEW principle of carbon arc operation, applied in the design of this lamp, provides an exceptionally efficient source of therapeutic radiation, capable of producing an erythema in less than one minute at a distance of three feet from the arc.

In the design of this lamp special attention has been given to simplicity of operation, convenience and adaptability. Its graceful proportions and attractive appearance are in keeping with conservative taste.

It can be connected to any standard convenience outlet supplying 115 volt alternating current.

The transformer enclosed in the base steps up the line current to 40 amperes at the arc.

The chromium plated reflector is designed for effective utilization of the radiation from the arc.

A filter of special, ultra-violet transmitting glass limits the output essentially to wave-lengths found in natural sunlight. This filter is easily removed when it is desired to utilize the shorter ultra-violet wave-lengths from the carbon arc.

FLEXIBILITY

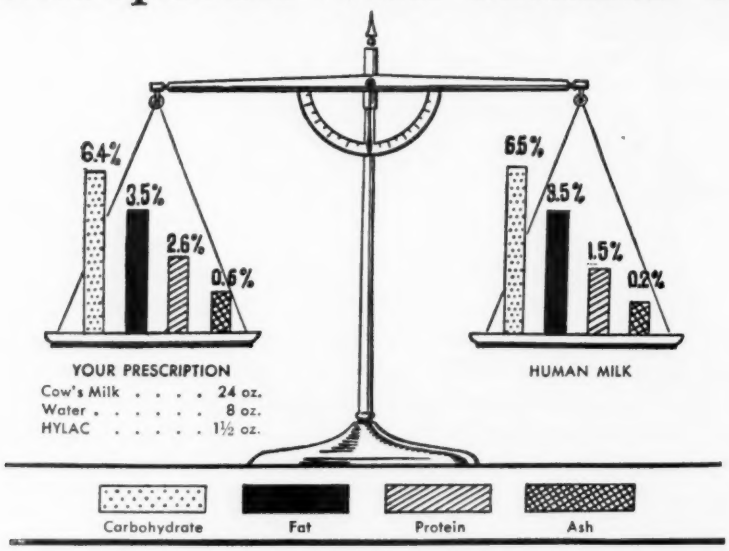
Three types of therapeutic radiation are available from this lamp:

- Close duplication of natural sunlight with Eveready "Sunshine" Carbons.
- Powerful ultra-violet emission with Eveready Therapeutic "C" Carbons.
- Strong infra-red radiation with Eveready Therapeutic "E" Carbons.

Write for Descriptive Bulletin

NATIONAL CARBON COMPANY, INC.
Carbon Sales Division, Cleveland, Ohio
Unit of Union Carbide UCC and Carbon Corporation
Sales Offices: New York Pittsburgh Chicago San Francisco

Your own Prescription
Compared with Human Milk



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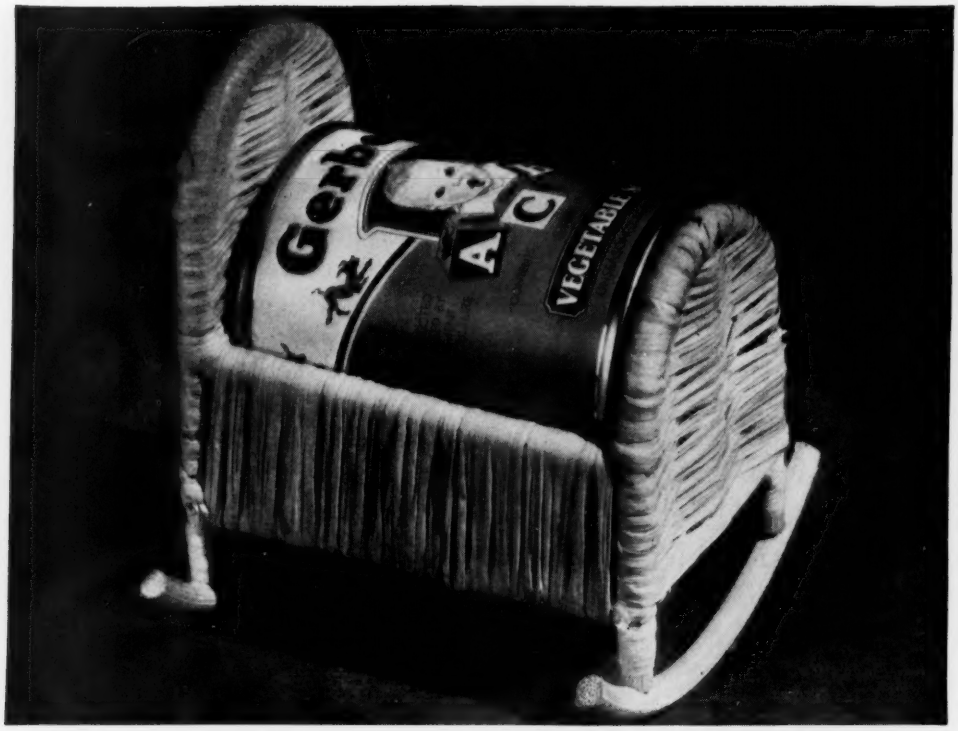
Write for Descriptive Bulletin

NATIONAL CARBON COMPANY, INC.
Carbon Sales Division, Cleveland, Ohio
Unit of Union Carbide UCC and Carbon Corporation
Sales Offices: New York Pittsburgh Chicago San Francisco



Rock-a-bye GERBER'S!

We call it "Shaker-Cooking." It is the new, improved method which makes Gerber's strained vegetables and cereal better than ever for babies.

The principle is simple. Just as the housewife *stirs* the contents of her saucepan, to insure more uniform cooking and prevent burning, so Gerber *shakes* the little sealed cans throughout the cooking process.

The old way of applying heat to motionless cans resulted in overcooking part of the contents, because it took too much time for heat to reach the center of the can and cook that part properly.

The cans of Gerber's products are shaken 140 times a minute. Cooking time is appreciably shortened with the result that the food is fresher in flavor, brighter in color—more appetizing!

Shaker-Cooking is an added justification for the confidence with which pediatrists prescribe Gerber's strained vegetables and cereal—foods specially prepared for babies, finely strained, unseasoned, and scientifically prepared and processed for highly efficient retention of minerals and vitamins.

● *Free to Physicians — for distribution to mothers*

"Baby's Book," by Harriet Davis, R. N., saves the physician's time by answering everyday questions asked by mothers about routine baby care. 32 attractive pages. Supplied free in quantity. Coupon will bring specimen copy for inspection.

Gerber's

Shaker-Cooked Strained Foods

Strained Vegetable Soup . . . Tomatoes . . . Green Beans . . . Beets . . . Carrots . . . Prunes . . . Spinach . . . Peas . . . 4½-oz. cans. *Strained* Cereal . . . 4½-oz. and 10¼-oz. cans.

GERBER PRODUCTS COMPANY, Fremont, Michigan
(In Canada, *Grown and Packed by* Fine Foods of Canada, Ltd., Tecumseh, Ont.)

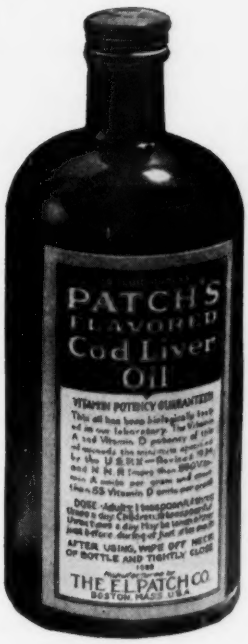
Please send me specimen copy of "Baby's Book," with the understanding that you will supply additional copies free upon request from me stating number needed. DC-12

Name .....

Street .....

City ..... *State* .....

SUNLESS DAYS



During the long Winter months, lack of sunshine suggests the need for increasing the regular intake of Vitamin D.

Patch's Flavored Cod Liver Oil provides a natural source of this important vitamin—standardized to meet the N.N.R. specifications.

In addition, Patch's also supplies a standardized amount of Vitamin A in compliance with N.N.R. standards.

EASY TO TAKE

Patch's Flavored Cod Liver Oil solves the great objection to cod liver oil—taste. By a special process Patch's has been rendered palatable, easy to take, even by the most finicky of patients.

You can prove this for yourself by sending us the attached coupon for a clinical trial bottle.

THE E. L. PATCH COMPANY

BOSTON, MASS.

ACCEPTED
AMERICAN MEDICAL ASSN.
Council on Pharmacy and Chemistry

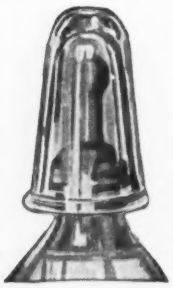
The E. L. Patch Co.
Stoneham 80, Dept. J.D.C. 12
Boston, Mass.

Gentlemen: Please send me a sample of Patch's Flavored Cod Liver Oil and literature.

Dr. .....

Address .....

City ..... State.....



BIG THINGS for a Little Cap to Do—

Physicians seldom fail to become deeply interested when they know how Steri-Seal Glass Caps work and what they do.

Simple to use—put them on *wet—snugly over the base of the nipple.* Right there is the secret of Steri-Seal's unequalled protection. Milk is bottled warm. In the refrigerator it cools, forms a vacuum inside the Steri-Seal Cap—an air-tight, germ-tight seal. A convincing test is easily made. Turn the bottle upside down—no air enters cap—no milk comes out.

That means sure protection for baby's feedings. And the work-saving side of the story is equally interesting. Write for free sample cap and descriptive circular.

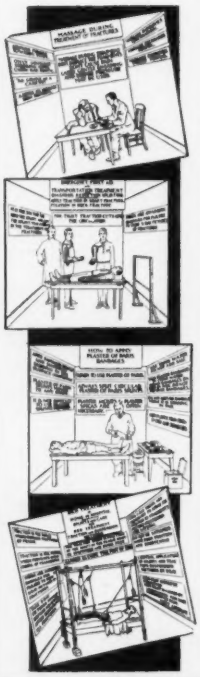
Steri-Seal Corporation

Dept. D **Columbus, Ohio**

STERI-SEAL

PRIMER ON FRACTURES

Third Edition—1933, Completely Revised



Acceptable methods of fracture treatment with large outline illustrations of the patient in proper position. Essential features of apparatus and methods are illustrated and described.

Contents:

How to Make and Apply Plaster-of-Paris Bandages; Fracture of the Hip—Neck of the Femur; Fracture of the Shaft of the Femur; Fracture of Lower Extremity; Fracture of the Tibia and Fibula; Fracture of the Clavicle; Fracture at the Shoulder—neck of Humerus; Compression Fracture of the Spine; Dislocation at the Shoulder; Fracture of the Forearm; Fracture of the Carpus, Metacarpus and Phalanges; Massage during Treatment of Fractures; Fracture of Skull; Splints and Accessories for Doctor's Automobile and Office.

Prepared by Cooperative Committee on Fractures. 68 pages. 8½ x 11. Printed on heavy ledger stock. Price, $1.00, postpaid.

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn St. Chicago, Il.

QUARTERLY CUMULATIVE INDEX MEDICUS

The One Complete Index to the World's Leading Medical Journals

The QUARTERLY INDEX covers more than 1,200 periodicals, and furnishes a simplified, systematic index of the timely literature available on any particular medical subject. Selective reading is made easy through this complete and ready reference. Have you availed yourself of this convenient time saver?

Arranged on Dictionary Plan

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The observations referred to covered only three prematures fed on different fats, but showed an average of 78.4% retention for olive oil as compared to only 52.5% retention for butter fat.

*Holt, Tidwell and Kirk, Studies on Fat Metabolism in Infants—Acta Pediatrica, Vol. XVI, 1933.

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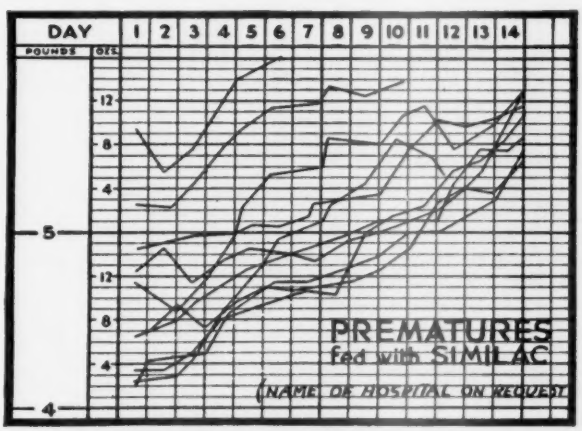

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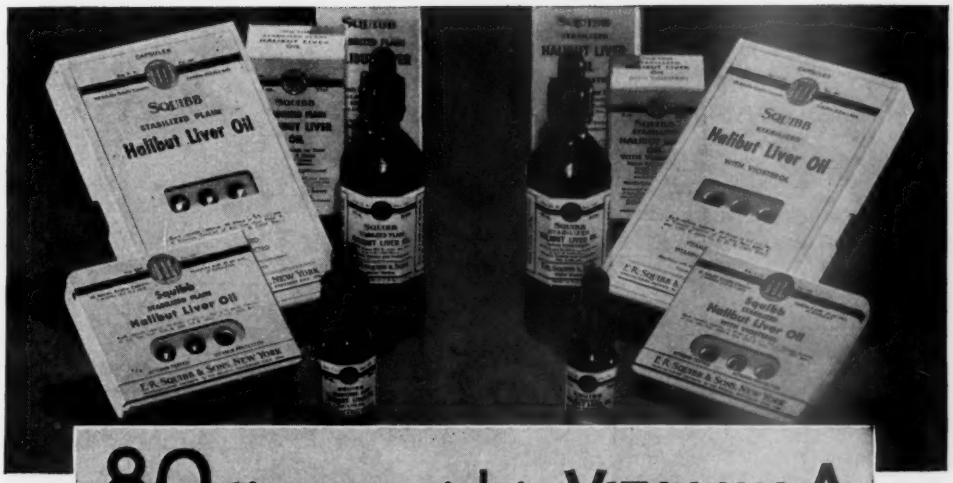

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NUTRITIONAL anemia was present in 45% of the breast-fed and 51% of the bottle-fed in a group of more than 1,000 infants studied by Mackay.[1] Although this anemia was of mild degree, *it was sufficient approximately to double the morbidity among the artificially fed.*

Anemia Prevalent

Commenting on this work, the British Advisory Committee on Nutrition writes, "This form of anaemia is prevalent among infants, especially those living under conditions of city life, and is attributed to a deficiency of available iron and possibly also of copper. Its most important feature is susceptibility to infection, particularly a liability to colds, otorrhoea, bronchitis, and enteritis, and a tendency for infections to become chronic."[2]

	IRON	COPPER
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Dextri-Maltose With Vitamin B,* 1 oz.	2.40	0.570
	3.41	0.736
Daily Requirement**	3.11	"traces"

*Essentially maltose and dextrins with extracts of wheat embryo and yeast.

It is generally agreed that breast milk and particularly cow's milk are markedly deficient in iron and copper. But when 1 oz. of Dextri-Maltose With Vitamin B is added to 14 oz. cow's milk, properly diluted (as at 1 month), the above increase in iron and copper results.

Iron, incorporated in powdered milk, should be given as a routine to bottle-fed infants, according to the recommendations of this committee in a report to the Ministry of Health.

Milk Deficient in Iron

Stored in the liver of the full-term infant is a supply of iron and copper theoretically sufficient for the first six months of life. But actually the reserve is subject to wide variation,[1] probably because of variations in the iron content of the mother's diet during pregnancy. Hill, for example, says, "If the mother is anemic herself, or if she has eaten little iron-containing food during the last months of pregnancy, her offspring is born with an insufficient iron deposit. . . ."[3]

	IRON	COPPER
Cow's Milk, 20 oz.	1.44 mg.	0.24 mg.
Dextri-Maltose With Vitamin B, 1½ oz.	3.60	0.855
Pablum, ¼ oz.	2.10	0.09
	7.14	1.185
Daily Requirement**	4.18	"traces"

When ¼ oz. of Pablum is fed to the 3-months-old infant receiving 20 oz. cow's milk and 1½ oz. Dextri-Maltose With Vitamin B, a significant increase in iron and copper takes place.

The trend is also toward the introduction of iron-rich solid foods at an early age. The iron content of many foods is variable, however. Leichsenring and Flor[4] found that children's diets planned to contain 5 and 8.5 mg. iron actually contained only 3.25 and 6.5 mg., respectively. Pablum, higher than most foods in iron and containing standardized amounts of this mineral can be administered as early as the third month. Clinical studies by Ross and Summerfeldt[6] and Crimm *et al*[6] show that Pablum is capable of increasing the hemoglobin percentage of growing children.

**The desirable iron intake for children, according to Rose *et al*, is 0.76 mg. per 100 calories. Infant of 1 month (8¼ lb.) and infant of 3 months (11¼ lb.), both require 50 calories per lb.[7]

[1-7] *Bibliography on request.*

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